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L83  ANSWER 1 OF 27  HCAPLUS  COPYRIGHT 2003 ACS
AN   2003:22845  HCAPLUS
DN   138:83340
TI   Compositions and methods for inhibiting human immunodeficiency
     virus infection by down-regulating human cellular genes, and
     inhibitor identification methods
IN   Holzmayer, Tanya A.; Dunn, Stephen J.
PA   Subsidiary No. 3, USA; Holzmayer, Andrew
SO   PCT Int. Appl., 44 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07D
CC   1-5 (Pharmacology)
     Section cross-reference(s): 3
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2003002528     A2    20030109      WO 2002-US20964  20020701 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI US 2001-302157P   P     20010629 <--
     US 2001-313252P   P     20010817 <--
AB   The invention provides methods for identifying human cellular genes and
     their encoded products for use as targets in the design of therapeutic
     agents for inhibiting or suppressing human immunodeficiency virus
     (HIV) infection.  The invention also provides methods for identifying
     protective compds., including immunizing agents that inhibit HIV
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infection. The invention further provides compds. for use in the treatment or prevention of HIV.

ST HIV infection inhibitor **screening** gene **protein** target

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (14-3-3, zeta, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Transport **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ABC (ATP-binding cassette) transporters, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Transport **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ADP/ATP carrier, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT ADP ribosylation factor
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ARF-3, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATIC, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATP1A1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATP5G2, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATP6E, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ArgBP2a, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (B56.gamma.1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (BBC-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (BMP1-6, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BTG-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C21orf4, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CCR4, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CCR7, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CSAD, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CSF3R, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CSNK1G2, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CTSD, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR4, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Csa-19, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DAP12, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DAP5, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DDX3, target; compns. and methods for inhibiting HIV infection by

down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DEAD/H Box 5, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DNA helicase, DEAD/H 9, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (E16, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (E1c, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (EF-1.delta., target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ERF-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Immunophilins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (FKBP (FK 506-binding **protein**), 1A, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GA17, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GABBR1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GNB2L1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GTP-binding, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HELO1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIP, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Animal cell line
(HL-60; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSHIP, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Heat-shock **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSP 90, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSPG, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HYPK, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IAP (integrin-assocd. **protein**), target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IEX-IL, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Annexins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(II, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(L1CAM, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LENG8, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAD-3/NFKBIA, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MIF, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MO25, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-.kappa.B (nuclear factor .kappa.B), binding subunit, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NME4, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NPM-RAR, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Nip 7-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2X1 receptor, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PABP (poly(A)-binding **protein**), target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Mononuclear cell (leukocyte)
(PBMC; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDCD4, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDIR, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RNA helicase, DDXL, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Retroviridae
(RTLV assocd. endogenous **retrovirus**, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Rox, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC11A1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SMG1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSR (signal sequence receptor), .beta. subunit, TRAP-.beta., target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSR (signal sequence receptor), .gamma., target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSR (signal sequence receptor), .delta., target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (T1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAP-1 (transporter in antigen processing 1), target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TCBA, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TCTP, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TID1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNF-.alpha. receptor, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Thromboxane receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TXA2R, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)
IT Cyclophilins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (U-snRNP-assocd., target; compns. and methods for inhibiting HIV

infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(URF 2, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(URF6, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(WBSCRI, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antigens CD11c, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Analysis
(biochem.; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT AIDS (disease)
Anti-AIDS agents
Antiviral agents
Apoptosis
Computer application
Computer program
Drug delivery systems
Drug screening
Drug targets
HeLa cell
Human
Human immunodeficiency **virus**
Macrophage
T cell (lymphocyte)
(compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Antisense oligonucleotides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Biological transport
(cotransport, sodium-D-glucose cotransport regulator, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytochrome b, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokine effector-inflammatory response, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(double strand break repair gene, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Elongation factors (**protein** formation)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(eEF-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Initiation factors (**protein** formation)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(eIF-3, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Initiation factors (**protein** formation)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(eIF-4B, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Initiation factors (**protein** formation)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(eIF4AI, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Initiation factors (**protein** formation)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(eIF4AII, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression, target overexpression; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT G **proteins** (guanine nucleotide-binding **proteins**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene CDC42, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene targeting
Genetic methods
(gene knockout; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT G **proteins** (guanine nucleotide-binding **proteins**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene rab7, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glutaredoxins, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(guanine nucleotide-releasing, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Ferritins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heavy subunit, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heterogeneous nuclear **ribonucleoprotein** A1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Ribonucleoproteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hnRNP (heterogeneous nuclear **ribonucleoprotein**), A2/B1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Immunoassay
PCR (polymerase chain reaction)
(in target expression measurement; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in target expression measurement; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(karyopherin, .beta.-subunit, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(keratin-related, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand-binding, FYN, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand-binding, HIV-1 tar binding **protein**, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand-binding, guanylate, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lymphocyte specific **protein** 1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel nuclear targeted, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nuclear U4A, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p18, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p40, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Tertiary structure
(**protein**, target **protein**; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT cDNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(random fragment expression library; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptin, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sodium-D-glucose cotransport regulator, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(suppressor element; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Human immunodeficiency **virus** 1
(tar binding **protein**, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(target **protein** inhibition assay; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Tertiary structure
(target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT CD44 (antigen)
CD68 (antigen)
CD69 (antigen)
Calnexin
Interleukin 1.beta.
Interleukin 6
Invariant chain (class II antigen)
Macrophage inflammatory **protein** 1.alpha.
Macrophage inflammatory **protein** 1.beta.
RANTES (chemokine)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ubiquitin-conjugating, UBE2M, target; compns. and methods for

inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Virus**
(**viral** stage assay; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(zinc finger factor 1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.2, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 37205-63-3, ATP synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ATP5E, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9028-04-0, NADH ubiquinone oxidoreductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B22 subunit, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 79747-53-8, **Protein** tyrosine phosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BDP-1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 78990-62-2, Calpain
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CAPNS1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 52660-18-1, Casein kinase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CSNK1E, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9037-42-7, DNA methyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNMT3A, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 306298-47-5, Dual-specificity **protein** phosphatase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DUSP1, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 127407-08-3, G **Protein**-coupled receptor kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPRK6, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 109136-49-4, Ubiquitin-specific protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HAUSP, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 335605-46-4, MAP kinase kinase 7
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(MAP2K7, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 267008-45-7, Misshapen/NIKs-related kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MINK, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 80449-02-1, **Protein** tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PTK2B, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9026-43-1, Serine/threonine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(STK10, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 342646-20-2, HD-PTP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9027-03-6, Cytochrome bc-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(core **protein**, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9054-89-1, Superoxide dismutase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoform 2, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9000-97-9, Aspartate aminotransferase 9001-16-5, Cytochrome oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mitochondrial, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 362479-32-1, **Protein** phosphatase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulatory, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9001-50-7, Glyceraldehyde 3-phosphate dehydrogenase 9001-88-1, Phosphorylase kinase 9013-10-9, Glucosamine-6-phosphate deaminase 9023-44-3, Tryptophanyl tRNA synthetase 9026-09-9, Phenol sulfotransferase 9028-06-2 9028-86-8, Aldehyde dehydrogenase 9030-22-2, Uridine phosphorylase 9031-02-1, 2-Oxoglutarate dehydrogenase 9031-48-5, Glucosyltransferase 9036-21-9, Phosphodiesterase 3B 9047-22-7, Cathepsin B 9067-83-8, CDP-diacylglycerol synthase 9073-99-8, Glucosidase II 9077-14-9, Squalene synthetase 37205-35-9, Arginyl tRNA synthetase 37277-59-1, O-Linked GlcNac transferase 60616-82-2, Cathepsin L 91755-78-1, CARM1 methyltransferase 115926-52-8, PI3 kinase 144941-32-2, Fgr tyrosine kinase 153190-61-5, TYK2 **protein** kinase 256474-93-8, **Protein** kinase CLK3 362674-81-5, **Protein** phosphatase 2A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 484096-47-1 484096-48-2 484096-49-3 484096-50-6 484096-51-7 484096-52-8
RL: PRP (Properties)
(unclaimed sequence; compns. and methods for inhibiting human

immunodeficiency **virus** infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (vacuolar proton ATPase proton channel subunit 6C, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 9014-08-8
RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.-, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

L83 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2003:5792** HCAPLUS
DN **138:61291**
TI Novel **bacteriophage** preparation for treatment of intracellular **bacterial** infections
IN Pasechnik, Vladimir; West, David
PA Regma Bio Technologies Ltd Nevada Usa, UK; Polyanskaya, Natasha
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-00
CC 63-5 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003000274	A2	20030103	WO 2002-GB2879	20020621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-15385 A 20010622

AB A **bacteriophage** prepn. is provided comprising a **bacteriophage** which is adapted to enter a eukaryotic **cell** and/or a eukaryotic cellular compartment, which **bacteriophage** is lytic towards at least one strain of **pathogenic bacteria** which may infect said **cell** or compartment, which **bacteriophage** is fused to, or linked to, or is adapted to express an annihilation moiety, which annihilation moiety is adapted when in the presence of at least one specific **pathogen** to cause or stimulate the **death** or inactivation of said **cell**; such that said **bacteriophage** prepn. is capable of causing or stimulating the **death** or inactivation of **cells** which are infected with said **pathogen**. The invention further comprehends a pharmaceutical compn. comprising such a **bacteriophage** prepn., formulated for administration to a patient in need thereof; method for producing the **death** or inactivation of a **cell** infected by a **pathogen** through the administration of such a **bacteriophage** prepn. thereto; and the use of such a **bacteriophage** prepn. in the manuf. of such a pharmaceutical compn., optionally for use in the treatment and/or the prophylaxis of a disease which is mediated or characterised by intracellular infection by a **pathogen**, including in particular tuberculosis, AIDS, HIV infection, and malaria.

ST **bacteria** intracellular **pathogen** drug delivery **bacteriophage**

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CS (circumsporozoite); **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT **Toxins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**anthrax**; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT Eukaryota
(**bacterial** intracellular infection of; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT AIDS (disease)
Antibacterial agents
Bacteriophage
Biological transport
Bordetella bronchiseptica
Bordetella pertussis
Brucella melitensis
Campylobacter
Chlamydia
Cytolysis
Drug delivery systems
Francisella tularensis
Haemophilus influenzae
Human
Human immunodeficiency **virus** 1
Klebsiella pneumoniae
Legionella pneumophila
Leishmania donovani
Listeria monocytogenes
Multidrug resistance
Mycobacterium avium
Mycobacterium tuberculosis
Phosphorylation, biological
Plasmodium falciparum
Protein degradation
Rickettsia prowazeki
Salmonella enteritidis
Salmonella typhimurium
Shigella
Simian immunodeficiency **virus**
Streptococcus group B
Streptococcus pneumoniae
(**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT Drosophila melanogaster
(homeodomain translocation **peptide** from; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT **Pathogenic bacteria**
(lysis of; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

IT **Protozoa**

(**pathogenic**; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)
IT **Apoptosis**
(stimulation of; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tat, of HIV-1; **bacteriophage** prepn. for treatment of intracellular **bacterial** infections)
IT 9001-92-7, Protease 80146-82-3, Preornithine carbamoyltransferase 192230-93-6, Procaspase 7 201556-11-8, Procaspase 3 264888-91-7, Apoptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)
IT 479540-98-2
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)
IT 24937-47-1, Polyarginine 25212-18-4, Polyarginine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bacteriophage** prepn. for treatment of intracellular **bacterial** infections)

L83 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:965027 HCAPLUS
DN 138:35038
TI Crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug **screening**
IN **Watowich, Stanley J.**; **Weaver, Scott C.**; **Davey, Robert A.**
PA Board of Regents, the University of Texas System, USA
SO U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12N009-64
ICS C12P021-02; C12N005-06; C12N009-20
NCL 435226000; 435069100; 435320100; 435325000; 435198000
CC 6-3 (General Biochemistry)
Section cross-reference(s): **1**, 3, 4, 10, 75
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002192799	A1	20021219	US 2001-981286	20011015 <--
PRAI US 2000-240187P	P	20001013 <--		

AB The present invention provides collections of **polypeptides** constructed using combinatorial libraries, where each **polypeptide** includes a region Xaan, wherein n is from about 5 to about 21, and each Xaa is independently a random **amino acid**. Each **polypeptide** includes a fragment of the Venezuelan equine encephalitis **virus** (VEEV) capsid **protein** C-terminal domain (CCD, residues 119-275). Polynucleotides encoding the **polypeptides**, are also provided, as are methods for identifying a **polypeptide** within a collection that prevents **cell death** after exposure to a **pathogen** or a **toxin**, and methods for identifying a **polypeptide** within a collection that binds a **pathogen**, a **toxin**, a **polypeptide**, or a polynucleotide. The present invention also provides methods for crystg. a **polypeptide**. Crystn. and crystal structure of the VEEV CCD is disclosed. Cloning combinatorial adaptein libraries into

packaging vectors is presented. This describes the insertion of a DNA oligonucleotide, which contains a stretch of random sequence, into the DNA sequence coding for the tat-CCD fusion **protein**, within a **retrovirus** packaging vector. This allows for the expression of a fusion **protein** that contains tat, CCD, and a random **peptide** inserted into the CCD sequence. The assays to identify the adapteins that protect **cells** and animals from RVFV are described. The ability of purified recombinant Tat-CCD carrier **protein** to cross **cell** membranes was examd.

ST VEEV capsid **protein** crystn crystal structure drug discovery **screening**; adaptein combinatorial library VEEV capsid **protein** drug discovery **screening**

IT Fusion **proteins** (chimeric **proteins**)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); **USES (Uses)**
(adaptein; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Fusion **proteins** (chimeric **proteins**)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); **USES (Uses)**
(capsid **protein** with cell peremeant **peptide** and Tat; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Proteins**
RL: BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); **USES (Uses)**
(capsid; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Rift Valley fever **virus**
(challenge of adaptein library-contg. cells with RVFV; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Genetic vectors
Molecular cloning
Murine leukemia **virus**
PCR (polymerase chain reaction)
Retroviral vectors
(cloning combinatorial adaptein libraries into packaging vectors; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Primers (nucleic acid)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cloning combinatorial adaptein libraries into packaging vectors; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Crystal growth
Crystal morphology
Crystal structure
Drug screening

Peptide library
Venezuelan equine encephalitis **virus**
(crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Polyoxyalkylenes, uses
RL: NUU (Other use, unclassified); USES (Uses)
(crystn. soln. contg.; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT DNA sequences
(for capsid **protein** and adapteins; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Protein** sequences
(of capsid **protein** and adapteins; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Virus**
(**pathogenic**, **screening** for **polypeptide** preventing **cell death** after exposure to **pathogen** or **toxin**; crystal structure of VEEV capsid **protein** C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

IT Biological transport
(permeation, of recombinant Tat-CCD carrier **protein** through cell membrane; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Cell death**
Pathogen
Pathogenic bacteria
Rickettsia
(**screening** for **polypeptide** preventing **cell death** after exposure to **pathogen** or **toxin**; crystal structure of VEEV capsid **protein** C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

IT **Toxins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**screening** for **polypeptide** preventing **cell death** after exposure to **pathogen** or **toxin**; crystal structure of VEEV capsid **protein** C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

IT **Antibacterial agents**
Antimicrobial agents
Antiviral agents
Fungicides
(**screening** for; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Antitoxins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**screening** for; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT Transcription factors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study,

unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(tat, fusion products with capsid **protein** and cell peremeant **peptide**; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT **Fungi**
(**zoopathogenic**, **screening** for **polypeptide** preventing **cell death** after exposure to **pathogen** or **toxin**; crystal structure of VEEV capsid **protein** C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

IT 478749-39-2DP, subfragments and variants are claimed
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(**amino acid** sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478749-43-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(**amino acid** sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478749-41-6P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(amion acid sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 188842-14-0P 189036-91-7P 191936-91-1P 478314-83-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(cell peremeant region; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 57-13-6, Urea, uses 7783-20-2, Ammonium sulfate, uses 7786-30-3, Magnesium chloride, uses 25322-68-3, Polyethylene glycol
RL: NUU (Other use, unclassified); USES (Uses)
(crystn. soln. contg.; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478749-40-5P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478749-42-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478749-38-1
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug **screening**)

IT 478750-94-6 478750-95-7 478750-96-8 478750-97-9 478750-98-0
478750-99-1 478751-00-7 478751-01-8 478751-02-9 478751-03-0
478751-04-1 478751-05-2 478751-06-3 478751-07-4 478751-08-5
478751-09-6 478751-10-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug **screening**)

IT 478751-11-0
RL: PRP (Properties)
(unclaimed **protein** sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug **screening**)

IT 478751-12-1 478751-13-2
RL: PRP (Properties)
(unclaimed sequence; crystal structure of VEEV capsid **protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug **screening**)

L83 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:906304 HCAPLUS
DN 138:12024
TI Construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents
IN Tan, Yin Hwee; Tan, Yee Joo; Lim, Siew Pheng; Lim, Seng Gee; Hong, Wan Jin; Goh, Phuay Yee
PA Institute of Molecular and Cell Biology, Singapore
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-705
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 9, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002094874	A2	20021128	WO 2002-CA762	20020524 <--
WO 2002094874	A3	20030220		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-12652 A 20010524 <--

AB The invention relates to a chimeric transmembrane **protein** designed to promote **viral** entry into cells, and a non-human transgenic animal or cells comprising such a **protein** and a method of infecting such cells and animals with a **virus**. The **protein** comprises: (i) an extracellular domain capable of binding a **virus**; and (ii) an intracellular internalization signal. The present inventors have engineered endocytosys and membrane anchoring signals into the C-terminus of the Ig heavy chain and have shown that these chimeric antibodies are displayed on the cell surface and undergo endocytosis. The inventors have shown that these cell surface antibodies can bind HIV-1 **virus** with high affinity which results in the internalization of the **virus** into a human kidney cell line. The present inventors have constructed two CD81 chimeric receptors by linking either the N- or C-terminus of CD81 with cytoplasmic domains of the transferrin receptor or the low d. **lipoprotein** receptor, resp., and have found that the CD81 chimeras have better internalization efficiency than wild-type CD81. The inventors have shown that the internalization efficiencies of these receptors is correlated with infectivity of cultured liver cells that are over-expressing either wild-type or chimeric CD81 receptors by HCV virions produced by a tetracycline-inducible cell culture system. The invention also relates to methods for testing and **screening** anti-**viral** agents.

ST chimeric transmembrane receptor **protein** antibody **virus** internalization **antiviral screening**; CD81 chimeric receptor design HCV internalization; Ig heavy chain chimeric design HIV1 internalization

IT Hybridoma
(902, for chimeric antibody construction; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Vaccines
(AIDS; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E2, chimeric **protein** extracellular domain contg. antibody to; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Asialoglycoprotein** receptors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(H1 subunit, chimeric **protein** contg. intracellular domain of; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Liver
(HCV expression in transgenic liver cell; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Animal cell line
(HuH-7, chimeric receptor expression in; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Lipoprotein** receptors

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LDL, chimeric **protein** contg. intracellular domain of; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Proteins**
RL: BPN (Biosynthetic preparation); **BUU (Biological use, unclassified)**; PRP (Properties); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(TAPA-1 (target of antiproliferative antibody, 1), chimeric **protein** extracellular domain contg.; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Vaccines
(anti-**viral**; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Transferrin receptors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric **protein** contg. intracellular domain of; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT CD4 (antigen)
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric **protein** extracellular domain contg.; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Antibodies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(coat, **viral**, chimeric receptor for; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Anti-AIDS agents**
Antiviral agents
Drug screening
Hepatitis B **virus**
Hepatitis C **virus**
Human
Human **coxsackievirus**
Human **herpesvirus**
Human immunodeficiency **virus**
Human immunodeficiency **virus** 1
Influenza **virus**
Molecular cloning
Protein engineering
Rabies **virus**
Rhinovirus
Rous sarcoma **virus**
Virus
(construction of chimeric transmembrane receptors and antibodies for

internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Fusion **proteins** (chimeric **proteins**)
Receptors
RL: BPN (Biosynthetic preparation); **BUU (Biological use, unclassified)**; PRP (Properties); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments, chimeric **protein** extracellular domain contg.; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Envelope **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, chimeric **protein** extracellular domain contg. antibody to; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Envelope **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp160env, chimeric **protein** extracellular domain contg. antibody to; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chains, chimeric **protein** extracellular domain contg. variable region; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Cell death**
Translation, genetic
(in assay for **screening** of anti-**viral** agents; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into **cells** and applications to **screening** of anti-**viral** agents)

IT Insulin-like growth factor II receptors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(insulin-like growth factor II/mannose phosphate, chimeric **protein** contg. intracellular domain of; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Protein** motifs
(internalization signal; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Biological transport
(internalization, receptor-mediated; construction of chimeric

transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chains, chimeric **protein** extracellular domain contg.; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Mannose receptors
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mannose 6-phosphate, chimeric **protein** contg. intracellular domain of; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Transgene
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(non-human animal; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Animal
(non-human transgenic; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT DNA formation
RNA formation
(**replication**, in assay for **screening** of anti-**viral** agents; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into **cells** and applications to **screening** of anti-**viral** agents)

IT Animal cell
(transgenic; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Protein** motifs
(transmembrane domain; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT **Anti-AIDS agents**
(vaccines; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT Infection
(**viral**; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT 477519-79-2, 1: PN: WO02094874 TABLE: 1 claimed DNA 477519-80-5, 2: PN: WO02094874 TABLE: 1 claimed DNA 477519-81-6 477519-82-7 477519-83-8
477519-84-9 477519-85-0 477519-86-1 477519-87-2 477519-88-3
477519-89-4 477519-90-7 477519-91-8 477519-92-9 477519-93-0
477519-94-1 477519-95-2 477519-96-3 477519-97-4 477519-98-5
477519-99-6 477520-00-6 477520-01-7 477520-02-8 477520-03-9
477520-04-0 477520-05-1
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

IT 477520-14-2 477520-15-3 477520-16-4 477520-17-5

RL: PRP (Properties)
(unclaimed sequence; construction of chimeric transmembrane receptors and antibodies for internalization of **virus** into cells and applications to **screening** of anti-**viral** agents)

L83 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:814359 HCAPLUS
DN 137:321247
TI **Screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using a conditionally replicating vector
IN Fuchs, Thilo M.
PA Creatogen Aktiengesellschaft, Germany
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): **1**, 10
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083940	A2	20021024	WO 2002-EP3874	20020408 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2001-108774	A	20010406	<--
EP 2001-110443	A	20010427	<--
EP 2001-120181	A	20010822	<--

AB This invention relates to a novel method for the identification of obligatory essential nucleic acid sequences, in particular **microbial** sequences. If a genome-representing nucleic acid sequence library of a microorganism of interest (also called fragment library) is established in a conditionally **replicating** vector, the method may comprise a genome satg. mutagenesis. An important feature of genome satg. mutagenesis according to the invention is that those genomic fragments which are identified and further investigated contain an obligatory essential nucleic acid sequence. This is an advantage in comparison to a "neg." approach like transposon-mutagenesis that identifies only gene loci which can be disrupted by insertional mutagenesis without loss of **cell viabilitiy**. Moreover, since every ORF in an operon will be mutagenized, polar effects can be studied rapidly, instead of analyzing an operon by time-consuming subsequent knock out steps. The invention can be applied to any microorganism of interest. Obligatory essential genes of Salmonella enterica typhimurium were identified using the method of invention. Further, a method for the identification of novel **antimicrobial** compds. using the obligatory essential nucleic acids and **proteins** encoded thereby is provided.
ST **antimicrobial** drug target **screening** genome saturing mutagenesis; **microbial** gene **antimicrobial** **screening** GSM conditionally replicating vector
IT Nucleic acid amplification (method)
(DNA, charaxterizing lethal integrants by; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(accA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(acrB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(adhE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(alaS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(aroA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(asnS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(aspS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(bcr, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Combinatorial library
Phage display library
(candidate drugs modified by applying tecniques of; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Peptidomimetics
(candidate drugs modified by; **screening** method for anti-

microbial drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cca, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT PCR (polymerase chain reaction)
(charaxterizing lethal integrants by; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cheA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(citE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(clpX, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Genome
(comparative genomics, identification of orthologs by; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Proteins**
RL: BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(complexes, contg. **protein** encoded by identified obligatory essential gene; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Genetic vectors
(conditionally replicating; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Fusion **proteins** (chimeric **proteins**)
RL: BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(contg. **protein** encoded by identified obligatory essential gene; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(copR, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(csdA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cstA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cyoE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dapE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ddlB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dfp, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dnaC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dnaK, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(dxs, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(engA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(eno, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fabB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fabG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fadL, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fic, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(figH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(folD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Genomic library
(fragment, genome-representing, established in conditionally replicating vector; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM)

using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ftsW, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ftsY, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ftsl, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fusA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gcd, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gloA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(glyQ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(glyS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(groE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing

mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gyrA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gyrB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hemE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hemH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hflB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hisF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hisS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(holA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Recombination, genetic
(homologous, insertional duplication mutagenesis by, in microorganism host transformed with conditionally replicating vector; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Bacteria (Eubacteria)**
Gram-negative **bacteria**
Gram-positive **bacteria** (Firmicutes)
Yeast
(host, identifying lethal integrants; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Microorganism**
(host, transformed with conditionally replicating vector; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hrpA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hslJ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hyaD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(icdA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Growth, **microbial**
(identifying agents inhibiting; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ileS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(imp, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(infB, identified, from S. enterica typhimurium; **screening**

method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Mutagenesis
(insertional duplication, GSM (genome-saturing mutagenesis); **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(katG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(kdsB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(kdtA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lpdA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lphH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lpxA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lysS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(metG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(metK, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mglB gene, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Cell death**
(**microbial**, identifying agents leading to; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally **replicating** vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mraY, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mrp, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(msbA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mukF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(murB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(murD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES

(Uses)
(murE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(murG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mutS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(napA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(narH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(narZ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nrfB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nusA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Proteins**
RL: ANT (Analyte); BSU (Biological study, unclassified); **BUU (Biological use, unclassified)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **USES (Uses)**
(obligatory essential gene-encoded, as drug targets; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Salmonella enterica typhimurium
(obligatory essential genes from; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM)

using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(obligatory essential, as drug targets; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Molecular cloning
(of identified obligatory essential genes; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ompN, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(origin of replication, conditionally replicating, vector comprising; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pabC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pagD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Antibiotics
(pharmaceutical compn. further comprising; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. further comprising; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(phoB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pmrG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(polA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(prc, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(prfB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pssA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pstS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(purB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(pyrG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rcsC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rec, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(recC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(recF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rep, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Genetic methods
(replica plating, identifying lethal integrants by; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rfaB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rfaL, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rfb, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rplC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rplE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES

(Uses)
(rplF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rplL, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rplO, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rplP, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpmJ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpoA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpoB, rpoC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpoD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpsE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological

use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpsG-rpsL, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rpsM, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrfD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rriC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrl, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrlA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrlD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrlE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrlH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological

use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrlX, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rrsH, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ruvA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological

use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sbcD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT **Antimicrobial agents**
Drug delivery systems
Drug screening
(**screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(secF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(secY, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(selD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Reporter gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(selectable marker, vector comprising; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sipA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sopA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(spiA, identified, from S. enterica typhimurium; **screening**

method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ssaU, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sseC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(thrS, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tmk, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Antibodies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to **protein** encoded by identified obligatory essential gene; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(trxA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(vacB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Plasmids
(vir, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(wca, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(wrbA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yaeT, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yafD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yaiY, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ybdN, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ybeX, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ybgO, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ybjT, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ycaC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yceF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ychK, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yci, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yciG, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ydiJ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yeaZ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yeeF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yfaX, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yfgE, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ygtA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yhbM, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yhbZ, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yidD, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yieE-yjeF, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yifB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yigC, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yjeA, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yjgN, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yjjl, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)
IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yliB, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)
IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yoa, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)
IT Gene, **microbial**
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ytfE, ytfP, identified, from S. enterica typhimurium; **screening** method for anti-**microbial** drug targets by genome-saturing mutagenesis (GSM) using conditionally replicating vector)

L83 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:755050 HCAPLUS
DN 137:274804
TI Positive selection system to **screen** for agents which block or activate intein splicing
IN Perler, Francine B.; Adam, Eric E.
PA USA
SO U.S. Pat. Appl. Publ., 54 pp., Cont.-in-part of U.S. 5,834,247.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-68
NCL 435006000
CC 6-3 (General Biochemistry)
Section cross-reference(s): **1**, 3, 9, 10, **63**
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142296	A1	20021003	US 1999-430221	19991029 <--
	US 6521425	B2	20030218		
	US 5834247	A	19981110	US 1997-811492	19970305 <--
	WO 2001032831	A2	20010510	WO 2000-US29596	20001027 <--
	WO 2001032831	A3	20020207		
	W: CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1226257	A2	20020731	EP 2000-973923	20001027 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	US 1997-811492	A2	19970305 <--		
	US 1992-4139	A2	19921209 <--		
	US 1993-146885	B2	19931103 <--		
	US 1995-496247	B2	19950628 <--		

US 1995-580555 B2 19951229 <--
US 1999-430221 A 19991029 <--
WO 2000-US29596 W 20001027 <--

AB Pos. selection systems that can be used tp **screen** for agents that control splicing of inteins in their native host **protein** (extein) or in homologous exteins. The selection system uses a host **cell** and a plasmid. The host **cell** has a chromosomal gene encoding either a drug-resistant form of a target enzyme or a wild-type target enzyme and the plasmid carries a gene encoding either a drug-sensitive form of the target enzyme, which is dominantly cytotoxic upon interaction with the drug, or a dominantly cytotoxic form of the target enzyme. The plasmid-borne gene contains an intein, and the inhibition or activation of splicing of the dominant cytotoxic form of the target enzyme by a given reagent results in the **survival** or **death** of the host **cell**. More specifically, pos. genetic selection systems which utilize the intein of the gyrA gene of **Mycobacterium** xenopi or the intein of the dnaB DNA helicase of **Mycobacterium** tuberculosis are provided. Similar systems utilizing native or homologous exteins and systems utilizing controllable inteins are provided, as are methods of controlling in vivo expression of **proteins** by modulating **protein** splicing with inhibiting or activating agents, and methods of controlling the delivery of **proteinaceous** drugs in vivo by modulating **protein** splicing.

ST **protein** splicing modulator **screening** intein extein pos selection; **Mycobacterium** intein splicing effector **screening** pos selection

IT Enzymes, biological studies
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA gyrases, gene gyrA, drug-resistant extein of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Mycobacterium tuberculosis**
(DnaB helicase intein of, **screening** for effectors of splicing of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Chemotherapy
(control of **protein** splicing in; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Toxins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**cytotoxins**, selection of effectors of intein splicing using; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(dnaB gene, for DnaB helicase; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Escherichia coli
(expression host; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Proteins**
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); **BUU (Biological use, unclassified)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(extein, gene for, use in reporter system; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Drug screening**
(for regulators of intein splicing; pos. selection system to

screen for agents which block or activate intein splicing)

IT DNA formation factors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(gene dnaB, M. tuberculosis, intein of, **screening** for effectors of splicing of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Gene targeting
(gene knockout, regulated intein splicing in control of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Mycobacterium leprae**
Mycobacterium xenopi
(gyrA DNA gyrase intein of, **screening** for effectors of splicing of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Gene, **microbial**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gyrA, of M. xenopi and E. coli; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Recombination, genetic
(homologous, inserting of intein gene into homologous extein gene using; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Cell death**
(host, activation of selectable form of target enzyme results in; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Cell proliferation**
(host, expression of target enzyme results in; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Combinatorial library
(in fragment of chicken .alpha.-spectrin; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Drug delivery systems
(injections, of modulators of **protein** splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Enzymes, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intein-contg., in selection system **screening** for intein splicing modulators; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Antimicrobial agents**
Tuberculostatics
(lead compds. as, modulators of **protein** splicing as, **screening** for; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Conformation
(loop, **protein**, as site of intein splicing, modeling of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Simulation and Modeling, biological
(of intein regions of **proteins** in design of temp.-sensitive splicing variants; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Drug delivery systems
(of **proteinaceous** drugs, controlling of, by modulating **protein** splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Genetic methods

(pos. genetic selection system, for intein splicing modulators; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Gene therapy
Molecular cloning
Post-translational processing
Protein engineering
Protein splicing
(pos. selection system to **screen** for agents which block or activate intein splicing)

IT Genetic selection
(pos., in **screening** for effectors of intein splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(precursor, natural or extein homolog, modulation of intein splicing in; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Drug delivery systems
(prodrugs, **proteins** as, intein splicing in activation of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(protease sensitive site, within extein, as intein insertion site; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Mutation
(renders cytotoxic extein; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Inteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**screening** for effectors of excision of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Temperature
(**screening** for range of, in modulation of **protein** splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Cytotoxicity
(**screening** for, in selection of effectors of intein splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT **Peptide** library
(**screening** of; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Phenotypes
(selectable, of host cell, in reporter system, for **screening** of modulators of **protein** splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Mutagenesis
(site-directed, of intein gene, to generate temp. sensitive intein; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Mutation
(temp.-sensitive, in GyrA intein gene; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Spectrins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological

study); USES (Uses)
(.alpha.-, **peptide** library derived from, **screening** for modulators of intein splicing; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Chicken (Gallus domesticus)
(.alpha.-spectrin from; pos. selection system to **screen** for agents which block or activate intein splicing)

IT Conformation
(.beta.-strand, B8, generation of temp. sensitive mutation in, of GyrA intein; pos. selection system to **screen** for agents which block or activate intein splicing)

IT 465565-77-9 465565-78-0 465565-79-1 465565-80-4 465565-81-5
465565-82-6 465565-83-7 465565-84-8 465565-85-9 465565-86-0
465565-87-1 465565-88-2 465565-89-3 465565-90-6 465565-91-7
465565-92-8 465565-93-9 465565-94-0 465565-95-1 465565-96-2
465565-97-3 465565-98-4 465565-99-5 465566-00-1 465566-01-2
465566-02-3 465566-03-4 465566-04-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; pos. selection system to **screen** for agents which block or activate intein splicing)

IT 465565-70-2 465565-71-3 465565-72-4 465565-73-5 465565-74-6
465565-75-7 465565-76-8 465566-05-6 465566-08-9 465566-09-0
RL: PRP (Properties)
(unclaimed **protein** sequence; pos. selection system to **screen** for agents which block or activate intein splicing)

IT 338971-91-8 338971-92-9 338971-93-0 338971-94-1 338971-95-2
338971-96-3 338971-97-4 338971-98-5 465566-06-7 465566-07-8
RL: PRP (Properties)
(unclaimed sequence; pos. selection system to **screen** for agents which block or activate intein splicing)

L83 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:637813** HCAPLUS
DN **137:180844**
TI Yeast Bax-responsive genes for drug target identification in yeast and **fungi**
IN Contreras, Roland Henri; Eberhardt, Ines; Luyten, Walter Herman Maria Louis; Reekmans, Rieka Josephina
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): **1**, 6, 10
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002064766	A2	20020822	WO 2001-EP15398	20011221 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2000-870318	A	20001222 <--		
	EP 2001-870002	A	20010104 <--		
	EP 2001-870003	A	20010109 <--		

AB The cDNAs for Saccharomyces cerevisiae genes responding to BAX gene

expression as well as the **proteins** encoded by these cDNAs are disclosed. Addnl., Candida albicans and human homologs of the S. cerevisiae genes/**proteins** are provided. The invention describes the use of nucleic acids and **proteins** which are involved in **apoptosis** in yeast or **fungi** for the prepn. of medicines for treating diseases assocd. with yeast or **fungi** or for the treatment of **proliferative** disorders or for preventing **apoptosis** in certain diseases. Methods are provided to identify compds. which selectively modulate the expression or functionality of said **proteins** in the same or a parallel pathway. Also provided are compds. as well as pharmaceutical compns., medicines and vaccines. The invention also comprises new nucleic acid sequences, probes and primers derived thereof, expression vectors and host **cells** transformed with said vectors, **polypeptides** and antibodies raised against said **polypeptides**.

ST sequence Saccharomyces Candida human Bax responsive gene cDNA **protein**; **apoptosis** gene **protein** Saccharomyces Candida human drug **screening**

IT Gene, animal
Gene, **microbial**
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(BAX-responsive; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BAX; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Candida albicans
Human
Saccharomyces cerevisiae
(Bax-responsive cDNAs/**proteins** of; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Nucleic acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense, to **apoptosis**-assocd. nucleic acids; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT **Cell proliferation**
(disorders of, treatment of; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Aspergillus fumigatus
Schizosaccharomyces pombe
(drug **screening** with recombinant; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT cDNA sequences
(for Saccharomyces cerevisiae, Candida albicans, and human Bax-responsive gene-encoded **proteins**)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for **apoptosis**-assocd. nucleic acids; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT **Apoptosis**
(genes assocd. with; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Aspergillus
Blastomyces dermatitidis
Botrytis
Candida
Cladosporium
Coccidioides immitis
Cryptococcus neoformans

Epidermophyton floccosum
Fusarium
Histoplasma capsulatum
Malassezia
Microsporum
Paracoccidioides brasiliensis
Sporothrix schenckii
Trichophyton
Zygomycetes
(infection by, treatment of; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Animal cell
(mammalian, recombinant, **apoptosis**-assocd. gene-expressing; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT **Proteins**
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **USES (Uses)**
(of BAX-responsive genes; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT **Protein** sequences
(of Saccharomyces cerevisiae, Candida albicans, and human Bax-responsive gene-encoded **proteins**)

IT **Bacteria** (**Eubacteria**)
Fungi
Yeast
(recombinant **apoptosis**-assocd. gene-expressing; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to **apoptosis**-assocd. **proteins**; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT Animal
(transgenic, **apoptosis**-assocd. gene-expressing; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT **Drug screening**
Fungicides
Vaccines
(yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 450436-44-9 450436-45-0 450436-46-1 450436-47-2 450436-48-3
450436-49-4 450436-50-7 450436-51-8 450436-52-9 450436-53-0
450436-54-1 450436-55-2 450436-56-3 450436-57-4 450436-58-5
450436-59-6 450436-60-9 450436-61-0 450436-62-1 450436-63-2
450436-64-3 450436-65-4 450436-66-5 450436-67-6 450436-68-7
RL: PRP (Properties)
(Unclaimed; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 450425-65-7 450425-67-9 450425-69-1 450425-71-5 450425-73-7
450425-75-9 450425-76-0 450425-78-2 450425-80-6 450425-82-8
450425-84-0 450425-86-2 450425-89-5 450425-91-9 450425-93-1
450425-95-3 450425-97-5 450425-99-7 450426-01-4 450426-03-6
450426-05-8 450426-07-0 450426-09-2 450426-11-6 450426-13-8
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450426-25-2 450426-27-4 450426-29-6 450426-31-0 450426-33-2
450426-35-4 450426-37-6 450426-39-8 450426-41-2 450426-43-4
450426-45-6 450426-47-8 450426-49-0 450426-51-4 450426-53-6
450426-55-8 450426-57-0 450426-60-5 450426-62-7 450426-64-9
450426-66-1 450426-69-4 450426-71-8 450426-73-0 450426-74-1

450426-75-2 450429-61-5 450429-62-6 450429-63-7 450429-64-8
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450430-30-5 450430-31-6 450430-32-7 450430-33-8 450430-34-9
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450430-45-2 450430-46-3 450430-47-4 450430-48-5 450430-49-6
450430-50-9 450430-51-0 450430-52-1 450430-53-2 450430-54-3
450430-55-4 450430-56-5 450430-57-6 450430-58-7 450430-59-8
450430-60-1 450430-61-2 450430-62-3 450430-63-4 450430-64-5
450430-65-6 450430-66-7 450430-67-8 450430-68-9 450430-69-0
450430-70-3 450430-71-4 450430-72-5 450430-73-6 450430-74-7
450430-75-8 450430-76-9 450430-77-0 450430-78-1 450430-79-2
450430-80-5 450430-81-6 450430-82-7 450430-83-8 450430-84-9
450430-85-0 450430-86-1 450430-87-2 450430-88-3 450430-89-4
450430-90-7 450430-91-8 450430-93-0, **Protein** Bax (synthetic
mouse gene BAX) 450432-16-3 450432-17-4 450432-18-5 450432-19-6
450432-20-9 450432-21-0 450432-22-1 450432-23-2 450432-24-3
450432-25-4 450432-26-5 450432-27-6 450432-28-7 450432-29-8
450432-30-1 450432-31-2 450432-32-3 450432-33-4 450432-34-5
450432-35-6 450432-36-7 450432-37-8 450432-38-9 450432-39-0
450432-40-3 450432-41-4 450432-42-5 450432-43-6 450432-44-7
450432-45-8, **Protein** (Candida albicans 343amino acid)
450432-46-9 450432-47-0 450432-48-1 450432-49-2 450432-50-5
450432-51-6 450432-52-7 450432-53-8 450432-54-9 450432-55-0
450432-56-1 450432-57-2 450432-58-3 450432-59-4 450432-60-7
450432-61-8 450432-62-9
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use);
ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**amino acid** sequence; yeast Bax-responsive genes
for drug target identification in yeast and **fungi**)

IT 450432-63-0 450432-64-1 450432-65-2 450432-66-3 450432-67-4
450432-68-5 450432-69-6 450432-70-9 450432-71-0 450432-72-1
450432-73-2 450432-74-3 450432-75-4 450432-76-5 450432-77-6
450432-78-7 450432-79-8 450432-80-1 450432-81-2 450432-82-3
450432-83-4 450432-84-5 450432-85-6 450432-86-7 450432-87-8
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450433-03-1 450433-04-2 450433-05-3 450433-06-4 450433-07-5
450433-08-6 450433-09-7 450433-10-0 450433-11-1 450433-12-2
450433-13-3 450433-14-4 450433-15-5 450433-16-6 450433-17-7
450433-18-8 450433-19-9 450433-20-2 450433-21-3 450433-22-4
450433-23-5 450433-24-6 450433-25-7, **Protein** (Candida
albicans 92-**amino acid**) 450433-26-8 450433-63-3
450433-64-4 450433-65-5 450433-66-6 450433-67-7 450433-68-8
450433-69-9 450433-70-2 450433-71-3 450433-72-4 450433-73-5
450433-74-6 450433-75-7 450433-76-8 450433-77-9 450433-78-0
450433-79-1 450433-81-5 450433-82-6 450433-83-7 450433-84-8
450433-85-9 450433-86-0 450433-87-1, **Protein** (Candida
albicans 95-**amino acid**) 450433-88-2, **Protein**
(Candida albicans 83-**amino acid**)

RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**amino acid** sequence; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 450425-64-6 450425-66-8 450425-68-0 450425-70-4 450425-72-6
450425-74-8 450425-77-1 450425-79-3 450425-81-7 450425-83-9
450425-85-1 450425-87-3 450425-88-4 450425-90-8 450425-92-0
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450426-04-7 450426-06-9 450426-08-1 450426-10-5 450426-12-7
450426-14-9 450426-16-1 450426-18-3 450426-20-7 450426-22-9
450426-24-1 450426-26-3 450426-28-5 450426-30-9 450426-32-1
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450428-63-4 450428-64-5 450428-65-6 450428-66-7 450428-67-8
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450429-03-5 450429-04-6 450429-05-7 450429-06-8 450429-07-9
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450431-08-0 450431-09-1 450431-10-4 450431-11-5 450431-12-6
450431-13-7 450431-14-8 450431-15-9 450431-16-0 450431-17-1
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450431-28-4 450431-29-5 450431-30-8 450431-31-9 450431-32-0
450431-33-1 450431-34-2 450431-35-3 450431-36-4 450431-37-5
450431-38-6 450431-39-7 450431-40-0 450431-41-1 450431-42-2
450431-43-3 450431-44-4 450431-45-5 450431-46-6 450431-47-7
450431-48-8 450431-49-9 450431-50-2 450431-51-3 450431-52-4

RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 450431-53-5 450431-54-6 450431-55-7 450431-56-8 450431-57-9
450431-58-0 450431-59-1 450431-60-4 450431-61-5 450431-62-6
450431-63-7 450431-64-8 450431-65-9 450431-66-0 450431-67-1
450431-68-2 450431-69-3 450431-70-6 450431-71-7 450431-72-8
450431-73-9 450431-74-0 450431-75-1 450431-76-2 450431-77-3
450431-78-4 450431-79-5 450431-80-8 450431-81-9 450431-82-0
450431-83-1 450431-84-2 450431-85-3 450431-86-4 450431-87-5
450431-88-6 450431-89-7 450431-90-0 450431-91-1 450431-92-2

450431-93-3 450431-94-4 450431-95-5 450431-96-6 450431-97-7
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450432-13-0 450432-14-1 450432-15-2 450433-46-2 450433-47-3
450433-48-4 450433-49-5 450433-50-8 450433-51-9 450433-52-0
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450433-80-4 450433-89-3 450433-90-6 450433-91-7 450433-92-8
450433-93-9 450433-94-0 450433-95-1
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 450430-92-9 450430-94-1 450430-95-2, DNA (synthetic mouse gene BAX fragment) 450430-96-3 450430-97-4 450430-98-5 450430-99-6
450431-00-2 450431-01-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

IT 155569-06-5 450436-36-9 450436-37-0 450436-38-1 450436-39-2
450436-40-5 450436-41-6 450436-42-7 450436-43-8
RL: PRP (Properties)
(unclaimed sequence; yeast Bax-responsive genes for drug target identification in yeast and **fungi**)

L83 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:595123** HCAPLUS
DN **137:135047**
TI In vitro cell interaction culture system for drug **screening**
IN Haeupl, Thomas; Kaps, Christian; Sittinger, Michael; Smolian, Heike
PA Germany
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM G01N033-50
ICS C12N005-06; C12N005-10; A61F002-30
CC 1-1 (**Pharmacology**)
Section cross-reference(s): 9, **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002061420	A2	20020808	WO 2002-DE353	20020128 <--
WO 2002061420	A3	20020926		
DE 10105420	A1	20020814	DE 2001-10105420	20010131 <--

W: US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI DE 2001-10105420 A 20010131 <--

AB The invention relates to an in vitro cell interaction culture system for testing and developing drugs, comprising a first cell culture made from pelletized and pre-cultivated mesenchymal cells, preferably articular pig chondrocytes, and a second cell culture which is applied to the first cell culture in a centrifugal manner and comprises human, immortalized synovial fibroblast cell lines (three-dimensional tissue engineering). The culture system can be used to study the effect of biol. and chem. substances, biomaterials, mech.-phys. influences and gene transfer systems for therapeutic purposes which, in particular are very close to conditions exhibited in vivo in healthy as well as in chronically diseased tissue for example joints and which can be used for identifying new access of therapy.

ST cell culture drug **screening** mesenchymal cell immortalized synovial fibroblast

IT Animal tissue culture
(EBV-transformed B-cells; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(HL-60; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(HSE; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(HUVEC; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(K4IM; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(Mono Mac 6; in vitro cell interaction culture system for drug **screening**)

IT Prion **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PrPSc; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
(U937; in vitro cell interaction culture system for drug **screening**)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autoantigens; in vitro cell interaction culture system for drug **screening**)

IT Medical goods
(biodegradable; in vitro cell interaction culture system for drug **screening**)

IT Joint, anatomical
(diseases; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue
(engineering; in vitro cell interaction culture system for drug **screening**)

IT Immunoassay
(enzyme-linked immunosorbent assay; in vitro cell interaction culture system for drug **screening**)

IT Transformation, neoplastic
(immortalization; in vitro cell interaction culture system for drug **screening**)

IT Animal tissue culture
Anti-inflammatory agents
Antibacterial agents
Antimicrobial agents
Antiviral agents
Apoptosis
Bone
Cartilage
Centrifugation
Chondrocyte
Culture media
DNA microarray technology
Dendritic cell
Disease models
Drug screening
Fibroblast
Gene therapy

Genetic engineering
Human
Intestine
Joint, anatomical
Kidney
Liver
Lymphocyte
Monocyte
Mouse
Necrosis
PCR (polymerase chain reaction)
Polymorphonuclear leukocyte
Protein microarray technology
Protozoa
Rat
Skin
Synovial membrane
Therapy
Virus
Wound healing
(in vitro cell interaction culture system for drug **screening**)

IT Agglutinins and Lectins
Antigens
Cytokines
Enzymes, biological studies
Epidermal growth factor receptors
Fibrins
Hormones, animal, biological studies
Lipopolysaccharides
Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro cell interaction culture system for drug **screening**)

IT Phagocyte
(macro; in vitro cell interaction culture system for drug **screening**)

IT Biodegradable materials
(medical; in vitro cell interaction culture system for drug **screening**)

IT Mesenchyme
(stem cell; in vitro cell interaction culture system for drug **screening**)

IT Animal
(transgenic; in vitro cell interaction culture system for drug **screening**)

IT Cell
(tumor; in vitro cell interaction culture system for drug **screening**)

IT 506-32-1, Arachidonic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(derivs.; in vitro cell interaction culture system for drug **screening**)

IT 9004-61-9, Hyaluronic acid 9005-32-7, Alginic acid 112887-68-0, Tomudex
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro cell interaction culture system for drug **screening**)

L83 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:595120** HCAPLUS
DN **137:139381**
TI HIV and CD4 transgenic animals and uses therefor
IN Bryant, Joseph L.; Reid, Michael C.; Davis, Harry G., Jr.
PA University of Maryland Biotechnology Institute, USA
SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-00
ICS A01K067-033; A01K067-27
CC 15-8 (Immunochemistry)
Section cross-reference(s): **1**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061416	A1	20020808	WO 2001-US31743	20011009 <--

PI W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-685256 A 20001010 <--

AB The invention provides transgenic rats comprising a **lentiviral** transgene, such as an HIV transgene. HIV transgenes can include gp120, rev, gag, pol, vif, vpr, vpu, tat, and nef. Also within the scope of the invention are cells and eggs from the transgenic animal. Further included are methods for identifying and **screening** of therapeutic compds. for preventing **lentiviral** infection and treating assocd. disease (e.g. AIDS). Assessment of HIV transgene expression can be used to identify anti-HIV agents and potential anti-AIDS drugs. Transgenic rats that express human CD4 can be used to assess HIV vaccines and anti-AIDS drugs that may be useful in humans.

ST HIV CD4 transgene rat drug **screening** disease model

IT Vaccines
(AIDS; HIV and human CD4 transgenic rats for testing of anti-HIV agents)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CCR5; HIV and human CD4 transgenic rats for testing of anti-HIV agents)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR4; HIV and human CD4 transgenic rats for testing of anti-HIV agents)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G; HIV and human CD4 transgenic rats for testing of anti-HIV agents)

IT AIDS (disease)
Anti-AIDS agents
Apoptosis
B cell (lymphocyte)
Disease models
Drug screening
Egg
Gamete and Germ cell
Human
Human immunodeficiency **virus**
Lentivirus
Macrophage
Mutagenesis
Sperm
T cell (lymphocyte)
Transformation, genetic
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Transgene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT **Viral** DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT **Viral** RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT gag **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(env; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gag; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene pol; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Envelope **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nef; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p24; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pol; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tat; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Rat
(transgenic; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT CD4 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transgenic; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT **Anti-AIDS agents**
(vaccines; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vif; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Infection
(**viral**; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vpr; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(vpu; HIV and human CD4 transgenic rats for testing of anti-HIV agents)
IT 9014-24-8, Rna polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV and human CD4 transgenic rats for testing of anti-HIV agents)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bryant; US 6156952 A 2000 HCAPLUS
(2) de; The Journal of Clinical Investigation 1997, V99(7), P1484 HCAPLUS
(3) Dickie, P; AIDS Research And Human Retroviruses 1996, V12(12), P1103 HCAPLUS
(4) Dickie, P; Virology 1991, V185, P109 HCAPLUS
(5) Hammer, R; US 5489742 A 1996 HCAPLUS
(6) Jolicoeur, P; US 5574206 A 1996 HCAPLUS
(7) Leonard, J; Science 1988, V242, P1665 MEDLINE
(8) The J David Gladstone Institute; WO 0039316 A1 2000 HCAPLUS
(9) Tinkle, B; The Joural of Clinical Investigation 1997, V100(1), P32 HCAPLUS

L83 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:539478** HCAPLUS
DN **137:103862**
TI RANTES in methods for ameliorating childhood **paramyxovirus** infections and for identifying susceptible individuals and drug **screening**
IN Holtzman, Michael J.
PA Washington University, USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-5 (**Pharmacology**)
Section cross-reference(s): 14, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002055019	A2	20020718	WO 2001-US45244	20011023 <--
WO 2002055019	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-243264P P 20001024 <--
AB Methods to treat **paramyxovirus** infection are disclosed, which comprise administering RANTES **protein** or an expression system therefor. Also disclosed are methods to identify individuals susceptible to **paramyxovirus** infection and methods to **screen** drugs. The invention centers on the discovery that the RANTES **protein** is able to prevent macrophage **cell death** and to enhance clearance of **virus** in infected subjects thus permitting the treatment of **paramyxovirus** infection using this **protein** or an expression system for it. Studies were done with mice.
ST RANTES ameliorating childhood **paramyxovirus** infection; drug **screening paramyxovirus** infection inhibitor; macrophage protection RANTES inhibition **paramyxovirus**
IT Chemokine receptors
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(CCR1, in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Chemokine receptors
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CCR5, in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT **Drug screening**
Gene therapy
Human
Lung
Macrophage
Paramyxovirus
Protein sequences
Risk assessment
Sendai **virus**
Susceptibility (genetic)
(RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT RANTES (chemokine)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Drug delivery systems
(aerosols; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT **Antimicrobial agents**
(against **paramyxovirus** infection; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Development, mammalian postnatal
(child; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Cell
(displaying CCR1 or CCR5 chemokine receptors, in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Gene, animal
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(for RANTES; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Nucleic acids
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(for RANTES; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Mutation
(in RANTES gene, risk for **paramyxovirus** infection in relation to; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Chemotaxis
(in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Lung, disease

(infection; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT **Apoptosis**
(inhibition, in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Mutagenesis
(random of RANTES, medicaments in relation to; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT Molecules
(small, as candidate medicaments; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flux, in drug **screening**; RANTES in treating **paramyxovirus** infections and identifying susceptible individuals and drug **screening**)

IT 443158-71-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed sequence; rANTES in methods for ameliorating childhood **paramyxovirus** infections and for identifying susceptible individuals and drug **screening**)

IT 443159-39-5 443159-40-8
RL: PRP (Properties)
(unclaimed sequence; rANTES in methods for ameliorating childhood **paramyxovirus** infections and for identifying susceptible individuals and drug **screening**)

L83 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:441364** HCAPLUS
DN **137:153892**
TI Monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-containing and serum-free media
AU Quesney, Sebastien; Marvel, Jacqueline; Marc, Annie; Gerdil, Catherine; Meignier, Bernard
CS Development Department, Campus Merieux, Marcy L'Etoile, F-69280, Fr.
SO Animal Cell Technology: From Target to Market, Proceedings of the ESACT Meeting, 17th, Tyloesand, Sweden, June 10-14, 2001 (2001), 213-216. Editor(s): Lindner-Olsson, Elisabeth; Chatzissavidou, Nathalie; Luellau, Elke. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69CRYK; ISBN: 1-4020-0264-5
DT Conference
LA English
CC 16-6 (Fermentation and Bioindustrial Chemistry)
AB The d. of **viable cells** in culture results from a balance between **cell proliferation** and **cell death**. The aim of this study was to characterize and compare these two phenomena in **Vero cell** cultures in one serum contg. medium (ScA) and one serum free medium (SfB) in bioreactors. ScA supported a higher maximal **viable-cell** d. (2.3 .times. 106 vs. 1.8 .times. 106 **cells**/mL). However, **cell** -cycle anal. showed that **cell** division was more active in SfB than in ScA. LDH release in the supernatant increased much earlier in SfB than in ScA (one vs. five days), but trypan blue counts showed no apparent difference in the **viability** of the cultures. **Apoptosis** , evidenced by annexin V-FITC/PI staining, could be detected in the population of suspension **cells** detached from microcarriers, but not among adherent **cells**; positivity of the TUNEL assay occurred later than that of the annexin V-FITC/PI staining. Our data indicate that the lower **cell** yield in SfB, compared with that in ScA, results

from a higher **cell death** rate. Apparently, **cells** die mostly from **apoptosis**.
ST **Vero cell** microcarrier culture growth **death** medium effect
IT Animal **cell** line
(**Vero**; monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-contg. and serum-free media)
IT Animal tissue culture
(microcarrier; monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-contg. and serum-free media)
IT **Apoptosis**
Cell death
Cell proliferation
Necrosis
(monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-contg. and serum-free media)
IT Culture media
(seru-free vs. serum-contg.; monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-contg. and serum-free media)
IT 9001-60-9, Lactate dehydrogenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monitoring growth and **death** of **Vero cells** cultivated in bioreactor with serum-contg. and serum-free media)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(4) Montagnon, J; Rev Infect Dis 1984, V6, P341
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L83 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:316408** HCAPLUS
DN **137:45090**
TI **Rickettsia**-macrophage interactions: host cell responses to **Rickettsia** akari and **Rickettsia** typhi
AU Radulovic, S.; Price, P. W.; Beier, M. S.; Gaywee, J.; Macaluso, J. A.; Azad, A.
CS Department of Microbiology and Immunology, University of Maryland, School of Medicine, Baltimore, MD, 21201, USA
SO Infection and Immunity (2002), 70(5), 2576-2582
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10, 15
AB The existence of intracellular **rickettsiae** requires entry, **survival**, and **replication** in the eukaryotic host **cells** and exit to initiate new infection. While endothelial **cells** are the preferred target **cells** for most **pathogenic rickettsiae**, infection of monocytes/macrophages may also contribute to the establishment of **rickettsial** infection and resulting **pathogenesis**. We initiated studies to characterize macrophage-**Rickettsia** akari and -**Rickettsia** typhi interactions and to det. how **rickettsiae survive** within phagocytic **cells**. Flow cytometry, microscopic anal., and LDH release demonstrated that R. akari and R. typhi caused negligible cytotoxicity in mouse peritoneal

macrophages as well as in macrophage-like **cell** line, P388D1. Host **cells** responded to **rickettsial** infection with increased secretion of proinflammatory cytokines such as interleukin-1.beta. (IL-1.beta.) and IL-6. Furthermore, macrophage infection with R. akari and R. typhi resulted in differential synthesis and expression of IL-.beta. and IL-6, which may correlate with the existence of biol. differences among these two closely related **bacteria**. In contrast, levels of gamma interferon (IFN-.gamma.), IL-10, and IL-12 in supernatants of infected P388D1 **cells** and mouse peritoneal macrophages did not change significantly during the course of infection and remained below the ELISA cytokine detection limits. In addn., differential expression of cytokines was obsd. between R. akari- and R. typhi-infected macrophages, which may correlate with the biol. differences among these closely related **bacteria**.

ST interleukin TNFalpha TGFbeta **Rickettsia** macrophage infection immune response; **Rickettsia** macrophage **apoptosis** NFkappaB transcription factor

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(I.kappa.B-.alpha. (NF-.kappa.B inhibitor .alpha.); expression of I.kappa.B-.alpha. mRNA in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(I.kappa.B-.alpha.-encoding; expression of I.kappa.B-.alpha. mRNA in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-.kappa.B (nuclear factor .kappa.B); expression of I.kappa.B-.alpha. mRNA in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages in relation to)

IT **Rickettsia akari**
Rickettsia typhi
(**Rickettsia**-macrophage interactions)

IT Macrophage
(activation; increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression of I.kappa.B-.alpha. mRNA in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT Immunity
Virulence (**microbial**)
(increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT Interleukin 1.beta.
Interleukin 6
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT **Apoptosis**
(increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages in relation to)

IT Macrophage
(infection; **Rickettsia**-macrophage interactions)

IT Cell activation
(macrophage; increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-; increased secretion of proinflammatory cytokines in **Rickettsia** akari- and **Rickettsia** typhi-infected macrophages)
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L83 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:293814** HCAPLUS
DN **136:320345**
TI **Protein** and DNA sequences of a novel **yatapoxvirus** **glycoprotein** gp38 and its uses in immune modulation
IN McFadden, Grant; Essani, Karim
PA Viron Therapeutics, Inc., Can.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): **1**, 10, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002031115	A2	20020418	WO 2001-US32136	20011011 <--
WO 2002031115	A3	20030213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002001174 A5 20020422 AU 2002-11744 20011011 <--
US 2002102535 A1 20020801 US 2001-976605 20011011 <--
PRAI US 2000-239354P P 20001011 <--
WO 2001-US32136 W 20011011 <--

AB The present invention discloses **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation. Specifically, the invention provides gp38 **polypeptides**, which play a role in immunomodulation, nucleic acid mols. encoding these **polypeptides**, and therapeutic and diagnostic methods employing these **polypeptides** and nucleic acid mols. The invention also provides methods for identifying compds. that modulate the biol. activities of gp38 nucleic acid mols. and **polypeptides**, and therapeutic methods employing these compds.

ST **yatapoxvirus glycoprotein** gp38 gene sequence immune modulation

IT Blood vessel, disease
(Raynaud's phenomenon, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Arthritis
(Reiter's syndrome, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Cell activation
(T cell, treatment of disorders of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Granulomatous disease
(Wegener's granulomatosis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Inflammation
Respiratory distress syndrome
(acute, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Leukocyte
(adhesion deficiency, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(against **Yatapoxvirus protein; protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Nose
(allergic rhinitis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Spinal column
(ankylosing spondylitis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Antiarteriosclerotics
(antiatherosclerotics, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Dermatitis
(atopic, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Stomach, disease

(atrophic gastritis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Anemia (disease)
(autoimmune hemolytic anemia, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Thyroid gland, disease
(autoimmune thyroiditis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Chemokines
Cytokines
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding **protein**; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Diagnosis
(cancer; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Rodentia
(cell, transgenic; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Human
Nonhuman primate
(cell; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Nervous system
(central, inflammatory disorder, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Autoimmune disease
(complications of AIDS, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Addison's disease
Asthma
Behcet's syndrome
Celiac disease
Dermatitis
Encephalitis
Food allergy
Graves' disease
Meningitis
Multiple sclerosis
Niemann-Pick disease
Psoriasis
Rheumatic fever
Sarcoidosis
Sjogren's syndrome
Transplant rejection
(diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Gene, **microbial**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(encoding yaba monkey tumor **virus glycoprotein** gp38; **protein** and DNA sequences of a novel

yatapoxvirus glycoprotein gp38 and its uses in immune modulation)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(for **Yatapoxvirus** gene; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Gene targeting
(gene knockout; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Kidney, disease
(glomerulonephritis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Abortion
(habitual, spontaneous, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Purpura (disease)
(idiopathic thrombocytopenic, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT **Proteins**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(immunomodulatory; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Intestine, disease
(inflammatory, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Diabetes mellitus
(insulin-dependent, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Heart, disease
(ischemia, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Antitumor agents
(leukemia; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Immune complexes
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(mediated disease, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Skin, disease
(pemphigoid, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Skin, disease
(pemphigus vulgaris, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT Skin, disease
(pemphigus, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38

and its uses in immune modulation)
IT Anemia (disease)
(pernicious anemia, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Muscle, disease
(polymyositis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Biliary tract
(primary biliary cirrhosis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT **Anti-AIDS agents**
DNA sequences
Dermatomyositis
Drug screening
Gene therapy
Genetic vectors
Immunomodulators
Immunostimulants
Immunosuppressants
Nucleic acid hybridization
Protein sequences
Swinepox **virus**
Tanapox **virus**
Test kits
Vaccines
Yaba monkey tumor **virus**
Yaba-like disease **virus**
Yatapoxvirus
(**protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Antisense oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Interleukin 2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Interleukin 5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Anti-inflammatory agents
(**protein** as; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Arthritis
(psoriatic arthritis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulatory; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune

modulation)
IT Artery, disease
(restenosis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Connective tissue
(scleroderma, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Shock (circulatory collapse)
(septic, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Dialysis
(syndrome, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Lupus erythematosus
(systemic, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Animal
(transgenic; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Rheumatoid arthritis
(treatment and diagnosis; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT **Apoptosis**
Cell proliferation
(treatment of disorders of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Wound healing
(treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Eye, disease
(uveitis, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Blood vessel, disease
(vasculitis, necrotizing, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Hepatitis
(**viral**, chronic active, diagnosis and treatment of; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)
IT 412021-72-8P 412110-21-5P 412110-35-1P 412110-37-3P, Gp38 (env **glycoprotein**) (swinepox **virus**)

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**amino acid** sequence; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT 412110-22-6P 412110-23-7P 412110-36-2P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

IT 412114-21-7, 8: PN: WO0231115 SEQID: 9 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; **protein** and DNA sequences of a novel **yatapoxvirus glycoprotein** gp38 and its uses in immune modulation)

L83 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:275723** HCAPLUS
DN **136:308522**
TI **Flaviviruse** and **Pestiviruse**-derive capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent
IN Weiner, David B.; Yang, Joo-Sung
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
ICI C12
CC 15-2 (Immunochemistry)
Section cross-reference(s): **1**, 3, 9, 10, **63**
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002028165	A2	20020411	WO 2001-US31355	20011004 <--
	WO 2002028165	A3	20020808		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002011490	A5	20020415	AU 2002-11490	20011004 <--
	US 2002123099	A1	20020905	US 2001-971806	20011004 <--
	US 2002164349	A1	20021107	US 2001-971980	20011004 <--
PRAI	US 2000-237885P	P	20001004 <--		
	WO 2001-US31355	W	20011004 <--		

AB This invention provides methods of inducing **cell death** with **Flavivirus** or **Pestivirus** capsid **protein**, such as West Nile **virus** (WNV) capsid **protein**, and functional fragments thereof. The invention also provides methods of treating patients suffering from diseases characterized by hyperproliferating **cells** (i.e. cancer) by administering pharmaceutical compns. WNV or encoding the same. Methods of identifying compds. which have anti-**viral** and/or anti-WNV and/or ant-**Flavivirus** and/or anti-**Pestivirus** capsid or other **protein** activity are disclosed. The invention also provides

vaccine compns. comprising capsid or other **proteins**, or fragments thereof, or nucleic acids encoding same, from WNV or other **virus** including **Flavivirus** or **Pestivirus** and a pharmaceutically acceptable carrier. The invention also provides diagnostic methods and kits for identifying individuals exposed to WNV or other **viruses** including **Flavivirus** or **Pestivirus**.

ST **Flavivirus Pestivirus** capsid **protein** cancer **antiviral**; cancer therapy diagnosis **apoptosis** **antiviral** agent; West Nile **virus** capsid **protein** vaccine

IT Animal cell line
(293; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Animal cell line
(RD; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Bioassay
(TUNEL anal.; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Annexins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(V, flow cytometry; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT **Drug screening**
(**antiviral** agent; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Biomarkers (biological responses)
(**apoptosis**; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT West Nile **virus**
(capsid **protein**; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT **Proteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(capsid; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Drug delivery systems
(carriers; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Medical goods
(containers; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT T cell (lymphocyte)
(cytotoxic, induction; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral**

agent)
IT Antitumor agents
Antiviral agents
DNA sequences
Flavivirus
HeLa cell
Human
Japanese encephalitis **virus**
Molecular cloning
Pestivirus
Protein sequences
Test kits
Vaccines
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT **Proteins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Antibodies
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Phosphatidylserines
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Cytometry
(flow, annexin V; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT DNA
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(free 3'-hydroxy termini; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Immunity
(humoral, antigen-specific; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Diagnosis
(immunodiagnosis; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT **Apoptosis**
(induction; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)
IT Lymphocyte
(infiltration; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Drug delivery systems
(injections, intratumoral; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Drug delivery systems
(injections; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Containers
(medical; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Infection
(**viral**, **Flavivirus** or **Pestivirus**; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma., intracellular; **flavivirus** and **pestivirus** -derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 410802-58-3
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**amino acid** sequence; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 251337-81-2P, GenBank AF202541
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 411207-77-7 411207-78-8 411207-79-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 410803-37-1, 7: PN: WO0228165 SEQID: 14 unclaimed DNA 410803-38-2, 8: PN: WO0228165 SEQID: 15 unclaimed DNA 410803-39-3, 9: PN: WO0228165 SEQID: 16 unclaimed DNA 410803-40-6 410803-41-7 410803-42-8 410803-43-9 410803-44-0 410803-45-1 410803-46-2 410803-47-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 410803-34-8 410803-35-9 410803-36-0 410803-48-4 410803-49-5
RL: PRP (Properties)
(unclaimed **protein** sequence; **flavivirus** and **pestivirus**-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

IT 411207-80-2 411207-81-3 411207-82-4
RL: PRP (Properties)
(unclaimed sequence; **flavivirus** and **pestivirus**

-derived capsid **proteins** for inducing **apoptosis**, diagnosing and treating cancer, and identifying **antiviral** agent)

L83 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:185165 HCAPLUS
DN 136:243571
TI Mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active molecules having the ability to alter and/or prevent and/or mimic the interaction of Vpr with ANT
IN Jacotot, Etienne Daniel Francois; Kroemer, Guido; Roques, Bernard Pierre; Edelmann, Lena; Hoebeke, Johan; Brenner-Jan, Catherine; Belzacq, Anne-Sophie
PA Institut Pasteur, Fr.; Centre National de la Recherche Scientifique; Institut National de la Sante et de la Recherche Medicale - INSERM; Universite de Technologie de Compiegne
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-155
CC 6-1 (General Biochemistry)
Section cross-reference(s): **1**, 10, 14
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002020570	A2	20020314	WO 2001-EP11316	20010911 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002015004	A5	20020322	AU 2002-15004	20010911 <--
US 2002068273	A1	20020606	US 2001-949650	20010912 <--
PRAI US 2000-231539P	P	20000911 <--		
US 2000-232841P	P	20000915 <--		
WO 2001-EP11316	W	20010911 <--		

AB The invention is directed to the induction of mitochondrial membrane permeabilization via the phys. and functional interaction of the HIV-1 **proapoptotic** Vpr **protein** with the mitochondrial inner membrane **protein** ANT (adenine nucleotide translocator, also called adenine nucleotide translocase or ADP/ATP carrier). HIV-1 Vpr (**viral protein** R) interacts with the permeability transition pore complex (PTPC) to trigger ANT pore formation and/or mitochondrial membrane permeabilization and consequent **cell death**. Reagents and methods fo inducing and/or inhibiting the binding of Vpr to ANT, mitochondrial membrane permeabilization, and **apoptosis** are provided.
ST HIV1 Vpr **protein** ANT mitochondria membrane permeabilization **apoptosis**
IT Transport **proteins**
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **USES (Uses)**
(ADP/ATP carrier; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)
IT **Proteins**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(Bcl-2; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Biological transport
(antiport; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Lipids, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(bilayer membrane or liposome; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Membrane, biological
(bilayer, planar; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT **Proteins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(gene vpr; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Diagnosis
(genetic; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT **Anti-AIDS agents**
Apoptosis
Cell death
Drug screening
Fluorescent indicators
Human
Human immunodeficiency **virus** 1
Liposomes
Molecular association
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Ion channel
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT **Peptides**, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Mitochondria
(membrane; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Membrane, biological
(mitochondrial; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Diagnosis

(mol.; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT Biological transport
(permeation, channel-mediated; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT 403842-76-2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

IT 10465-78-8, Diamide 17754-44-8, Atractyloside 72093-21-1, Mastoparan
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of **screening** active mols. altering, preventing or mimicking interaction of Vpr with ANT)

L83 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:18833** HCAPLUS
DN **136:383635**
TI Strategies for survival of intracellular **pathogens**
AU McDonough, Kathleen A.
CS Wadsworth Center, Albany, NY, USA
SO Molecular Medical Microbiology (2002), Volume 1, 755-786. Editor(s): Sussman, Max. Publisher: Academic Press, San Diego, Calif. CODEN: 69CDO2
DT Conference; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10
AB A review discusses the strategies used by the intracellular **bacterial pathogens** that **survive** against **microbicidal** capabilities of phagocytes. It focuses on **bacterium**-macrophage interactions because macrophages are the phagocytes most often exploited by **bacterial pathogens**, and have been most studied by those interested in **microbial pathogenesis**. The interactions between **bacterial pathogens** and their host **cells** are complex, and is just beginning to be understood. (c) 2002 Academic Press.
ST review intracellular **bacteria** macrophage **pathogenesis**
IT Respiration, animal
(burst; strategies for survival of intracellular **pathogens**)
IT **Pathogen**
(intracellular; strategies for survival of intracellular **pathogens**)
IT Organelle
(phagosome; strategies for survival of intracellular **pathogens**)
IT **Apoptosis**
Brucella
Chlamydia
Ehrlichia
Francisella
Legionella
Listeria
Lysosome
Macrophage
Mycobacterium
Pathogenic bacteria

Phagocytosis
Rickettsia
Salmonella
Shigella
(strategies for survival of intracellular **pathogens**)

RE.CNT 267 THERE ARE 267 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L83 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:435276** HCAPLUS
DN **135:29915**
TI Cloning of cDNA encoding a novel PROST-Ets **polypeptide** of human and its use in the diagnosis and treatment of prostate cancer
IN Harkins, Richard; Lin, Richard J.; Luke, May; Monteclaro, Felipe; Parkes, Deborah; Parry, Gordon; Steinbrecher, Renate; Van Heuit, Pamela Toy; Xuan, Jian-ai
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-47; C12N005-10; C07K016-18; A61K047-48; G01N033-68; C12N015-11; A61K031-7088
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): **1**, 6, 14, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001042472	A2	20010614	WO 2000-US42295	20001129 <--
	WO 2001042472	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1234037	A2	20020828	EP 2000-992356	20001129 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002002542	A	20020729	NO 2002-2542	20020529 <--

PRAI US 1999-168182P P 19991130 <--
US 2000-718159 A2 20001121 <--
WO 2000-US42295 W 20001129 <--

AB The present invention relates to cDNA encoding novel transcription factor **polypeptides**, designated PROST-Ets of human, methods for producing the **polypeptides**, expression vectors and genetically engineered host cells for expression of the **polypeptides**. It is a further object of the invention to provide antibodies which are highly selective for PROST-Ets **polypeptides**, or fragments thereof, and which may be employed in a method for diagnosis and/or detection of PROST-Ets expression, which may be assocd. with prostate cancer. The invention further relates to methods for utilizing the polynucleotides and **polypeptides** in research, diagnosis, and therapeutic applications.

ST human **protein** PROSTEts cDNA sequence expression; prostate cancer diagnosis drug immunotherapy human

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(DNA; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(PROST-Ets; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(PROST-Ets; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Animal tissue
Body fluid
Chromophores
Disease, animal
Drug screening
Drugs
Fluorescent substances
Genetic engineering
Immunoassay
Immunotherapy
Molecular cloning
Proliferation inhibition
Protein sequences
Radioactive substances
cDNA sequences
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT **Abrins**
Glucocorticoids
Radionuclides, biological studies
Ribozymes
Ricins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Enzymes, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Antisense oligonucleotides
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT **Toxins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**diphtheria**; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT RNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(encoding PROST-Ets; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Cytotoxic agents
(etoposide, tenoposide, and PE40; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Pseudomonas
(**exotoxin** (PE)A; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT **Toxins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**exotoxins**, (PE)**A**, of Pseudomonas; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, Fv, F(ab') and F(ab')2; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT **Cell death**
(from therapeutic agent of immunoconjugate; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(genomic; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Drug delivery systems
(immunoconjugates; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

IT Neoplasm
(metastasis; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT Diagnosis
(mol.; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monoclonal; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT DNA
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(primer; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT **Cell proliferation**
(prostate tumor; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT 343695-12-5
RL: PRP (Properties)
(Unclaimed; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT 257856-42-1D, Subfragments are claimed 343630-98-8 343630-99-9 343631-00-5
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**amino acid** sequence; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT 50-76-0, Actinomycin D 57-22-7, Vincristine 64-86-8, Colchicine 120-12-7D, Anthracene, dihydroxy dione derivs., biological studies **564-25-0**, Doxycycline 865-21-4, Vinblastine 1239-45-8, Ethidium bromide 1404-00-8, Mitomycin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 33069-62-4, Taxol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT 343694-58-6 343694-59-7 343694-60-0 343694-61-1D, Subfragments are claimed
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)
IT 343695-09-0 343695-10-3 343695-11-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; cloning of cDNA encoding novel PROST-Ets **polypeptide** of human and its use in diagnosis and treatment of prostate cancer)

L83 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:417128** HCAPLUS
DN **135:2558**
TI Method for producing adherent animal cells
IN Gerdil, Catherine

PA Aventis Pasteur, Fr.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM C12N005-00
CC 9-11 (Biochemical Methods)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001040443	A2	20010607	WO 2000-FR3377	20001204
WO 2001040443	A3	20011227		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2801900	A1	20010608	FR 1999-15303	19991203
EP 1238057	A2	20020911	EP 2000-985397	20001204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI FR 1999-15303	A	19991203	
WO 2000-FR3377	W	20001204	

AB The invention concerns a culture medium contg. a polyvinylpyrrolidone as substitute for the serum of animal origin for producing animal or human adherent **cells** under stirring by increasing the **cell proliferation** or by decreasing **cell death** rate. The medium is also suitable for producing **viruses.**
ST adherent animal cell culture medium polyvinylpyrrolidone
IT Animal cell line
(MRC-5; method for producing adherent animal cells)
IT Animal cell line
(**Vero**; method for producing adherent animal cells)
IT **Cell death**
(decrease of; method for producing adherent animal **cells**)
IT **Cell proliferation**
(increase of; method for producing adherent animal **cells**)
IT Animal cell line
Cell adhesion
Culture media
Hepatitis A **virus**
Human **poliovirus**
Measles **virus**
Virus
(method for producing adherent animal cells)
IT Mixing
(stirring; method for producing adherent animal cells)
IT 9003-39-8, Polyvinylpyrrolidone 9004-54-0, Dextran, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method for producing adherent animal cells)

L83 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:338675 HCAPLUS
DN 134:349697
TI **Screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins
IN Perler, Francine B.; Adam, Eric E.
PA New England Biolabs, Inc., USA

SO PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 9, 10, 63
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2001032831	A2	20010510	WO 2000-US29596	20001027	<--
	WO 2001032831	A3	20020207			
	W: CA, JP					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 2002142296	A1	20021003	US 1999-430221	19991029	<--
	US 6521425	B2	20030218			
	EP 1226257	A2	20020731	EP 2000-973923	20001027	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
PRAI	US 1999-430221	A	19991029	<--		
	US 1997-811492	A2	19970305	<--		
	WO 2000-US29596	W	20001027	<--		

AB In accordance with the present invention, there are provided selection systems and methods for **screening** for mutations or agents that control splicing of inteins (also known as intervening **protein** sequence or IVPS) in their native host **protein** (extein) or in homologous exteins. The agents includes, but not limited to, a **peptide** (free or displayed on a scaffold such as chicken .alpha.-spectrin), a **peptide** deriv., a natural product or a synthetic mol. Specifically, there are provided pos. genetic selection systems for the **screening** of agents which inhibit or activate **protein** splicing which comprise: a host **cell** contg. a chromosomal gene encoding either a drug-resistant form of a target enzyme or a wild-type target enzyme, and a plasmid-borne gene encoding either a drug-sensitive form of the target enzyme, which is dominantly cytotoxic upon interaction with the drug, or a dominantly cytotoxic form of the target enzyme. In these systems the plasmid-borne gene contains an intein, and the inhibition or activation of splicing of the dominant cytotoxic form of the target enzyme by a given reagent results in the **survival** or **death** of the host **cell**. More specifically, pos. genetic selection systems which utilize the M. xenopi GyrA (gyrase A) intein or M. tuberculosis DnaB helicase intein are provided. Similar reporter systems utilizing native or homologous exteins and systems utilizing controllable inteins (or controllable intervening **protein** sequences (CIVPS)) are provided, as are methods of controlling in vivo expression of **proteins** by modulating **protein** splicing with inhibiting or activating agents, and methods of controlling the delivery of **proteinaceous** drugs in vivo by modulating **protein** splicing.

ST **protein** splicing modulator **screening** intein extein; **Mycobacterium** tuberculosis DnaB intein splicing **antimicrobial**

IT Enzymes, biological studies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(DNA gyrases, GyrA, Ser83 mutant, of E. coli, drug-resistant extein for; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Enzymes, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(DNA gyrases, GyrA, of M. xenopi, intein from; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Mycobacterium tuberculosis**
(DnaB helicase, intein from, **screening** for **antimicrobials** against; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Mycobacterium xenopi**
(GyrA (gyrase A), intein from; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Mycobacterium leprae**
(GyrA intein from, **screening** for **antimicrobials** against; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Gene, **microbial**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(IVPS, for intein; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Inteins
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(IVPS, genes for; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Escherichia coli
(**Mycobacterium** gyrA or dnaB intein gene cloned into resp. gyrA or dnaB extein gene of; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Peptide** library
(agents from; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Chemotherapy
(control of **protein** splicing for, CIVPS (controllable inteins) for; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Drug screening**
(controllable intein (CIVPS); **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(controllable, use in selection system; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Gene, **microbial**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(dnaB gene, for DnaB helicase; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Cytotoxicity
(dominant, intein contg. enzyme with, extein with, host cell encoding; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Drugs

(dominantly cytotoxic enzyme upon interaction with, use in pos. selection system; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Proteins**, specific or class
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); **BUU (Biological use, unclassified)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); **USES (Uses)**
(extein, (mature **protein** after intein splicing), gene for, use in reporter system; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Reporter gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for any extein with tractable phenotype; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT DNA formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(gene dnaB, of M. tuberculosis, intein from, R231C mutation in extein of; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Genetic methods
(gene knockout, controllable; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Animal tissue
(gene therapy in, using modulators of **protein** splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Gene, **microbial**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gyrA, of M. xenopi and E. coli; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Recombination, genetic
(homologous, inserting of intein gene into homologous extein gene using; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Cell death**
(host, activation of selectable form of target enzyme results in; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Cell proliferation**
(host, expression of target enzyme results in; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Combinatorial library
(in fragment of chicken .alpha.-spectrin; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Drug delivery systems
(injections, of modulators of **protein** splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Antimicrobial agents**
Tuberculostatics
(lead compds. as, modulators of **protein** splicing as, **screening** for; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Conformation
(loop, **protein**, between B8 and B9 .beta.-strands, generation of temp. sensitive mutation in, of GyrA intein; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Conformation
(loop, **protein**, within extein, as intein insertion site; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Drug delivery systems
(of **proteinaceous** drugs, controlling of, by modulating **protein** splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Genetic methods
(pos. genetic selection system, for intein splicing modulators; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(precursor, natural or extein homolog, modulation of intein splicing in; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(protease sensitive site, within extein, as intein insertion site; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Mutation
(renders cytotoxic extein; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Gene therapy
Molecular cloning
Post-translational processing
Protein engineering
Protein splicing
(**screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Temperature
(**screening** for range of, in modulation of **protein** splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Phenotypes
(selectable, of host cell, in reporter system, for **screening** of modulators of **protein** splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Mutagenesis
(site-directed, of intein gene, to generate temp. sensitive intein; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Transformation, genetic
(systemic, with vector encoding inactive drug; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Drug resistance
(target enzyme with, host cell encoding; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)
IT Enzymes, biological studies

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target, non-selectable and selectable (intein contg.) forms of, host cell encoding; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Mutation
(temp.-sensitive, in M. xenopi GyrA intein gene; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT **Cell**
(**viability**, host, inhibition of splicing of cytotoxic **protein** results in; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Spectrins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(.alpha.-, as scaffold, for **peptide** library, in **screening** of modulators of intein splicing; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Chicken (Gallus domesticus)
(.alpha.-spectrin from; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT Conformation
(.beta.-strand, B8, generation of temp. sensitive mutation in, of GyrA intein; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 339211-50-6P 339211-52-8P 339211-53-9P
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**amino acid** sequence; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 339211-18-6 339211-47-1 339211-48-2 339211-49-3
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**amino acid** sequence; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 339211-51-7, .alpha.-Spectrin (Gallus domesticus fragment)
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(**amino acid** sequence; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-91-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(clone pEA814, inhibition of M. tuberculosis DnaB splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-92-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clone pEA815, inhibition of M. tuberculosis DnaB splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-93-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clone pEA816, inhibition of M. tuberculosis DnaB splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-94-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clone pEA817, inhibition of M. tuberculosis DnaB splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-95-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clone pEA818, inhibition of M. tuberculosis DnaB splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-96-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clone pEA818rev, inhibition M. tuberculosis DnaB of splicing by; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 338971-97-4 338971-98-5
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(intein insertion site, in GyrA; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

IT 339214-05-0 339214-06-1 339214-07-2 339214-08-3 339214-09-4
339214-10-7 339214-11-8 339214-12-9 339214-13-0 339214-14-1
339214-15-2 339214-16-3 339214-17-4 339214-18-5 339214-19-6
339214-20-9 339214-21-0 339214-22-1 339214-23-2 339214-24-3
339214-25-4 339214-26-5 339214-27-6 339214-28-7 339214-29-8
339214-30-1 339214-31-2 339214-32-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; **screening** and use of agents which block or activate intein splicing utilizing natural or homologous exteins)

L83 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:31627** HCAPLUS
DN **134:111252**
TI **Apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines
IN Contreras, Roland Henri; De Backer, Marianne Denise; Luyten, Walter Herman Maria Louis; Malcorps, Isabelle Karin Luc; Nelissen, Bart Jozef Maria; Reekmans, Rieka Josephina
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): **1**, 6, 10, 15
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2001002550	A2	20010111	WO 2000-BE77	20000703 <--
	WO 2001002550	A3	20011115		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1196635	A2	20020417	EP 2000-943491	20000703 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003504013	T2	20030204	JP 2001-508323	20000703 <--
	NO 2002000011	A	20020102	NO 2002-11	20020102 <--
PRAI	EP 1999-870141	A	19990701 <--		
	WO 2000-BE77	W	20000703 <--		

AB The invention describes the use of nucleic acids and **polypeptides** which are involved in a pathway eventually leading to programmed **cell death** of yeast or **fungi** for the prepn. of a medicament for treating diseases assocd. with yeast or **fungi** or for the treatment of **proliferative** disorders or for preventing **apoptosis** in certain diseases. Methods are provided to identify compds. which selectively modulate the expression or functionality of said **polypeptides** in the same or a parallel pathway. Also provided are compds. as well as pharmaceutical compns., medicaments and vaccines. The invention also comprises new nucleic acid sequences, probes and primers derived thereof, expression vectors and host **cells** transformed with said vectors, **polypeptides** and antibodies raised against said **polypeptides**. Thus, cDNAs corresponding to Saccharomyces cerevisiae genes modulated by Bax gene expression were identified using DNA arrays. Candida albicans cDNAs homologous to the Saccharomyces cDNAs are also presented.

ST sequence Candida Saccharomyces Bax regulated gene **protein**; **apoptosis** related gene Candida Saccharomyces drug **screening**; vaccine **fungicide apoptosis** related gene Candida Saccharomyces

IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax, yeast genes modulated by; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(anti-**apoptosis** gene product; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT Nucleic acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense, **apoptosis** genes-regulating; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT **Apoptosis**
Aspergillus
Aspergillus fumigatus
Blastomyces dermatitidis
Botrytis
Candida
Candida albicans
Cladosporium

Coccidioides immitis
Cryptococcus neoformans
Drug screening
Epidermophyton floccosum
Fungi
Fungicides
Fusarium
Histoplasma capsulatum
Malassezia
Microsporum
Paracoccidioides brasiliensis
Saccharomyces cerevisiae
Schizosaccharomyces pombe
Sporothrix schenckii
Trichophyton
Vaccines
Yeast
Zygomycetes
(**apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT **Cell proliferation**
(drugs for treatment of; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for **apoptosis**-related nucleic acids; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT cDNA sequences
(for **apoptosis**-related **proteins** of Saccharomyces cerevisiae and Candida albicans)

IT Animal cell
(mammalian, **apoptosis** gene-modified; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT **Protein** sequences
(of **apoptosis**-related **proteins** of Saccharomyces cerevisiae and Candida albicans)

IT 82030-08-8, Histone H 2A2 (Saccharomyces cerevisiae) 86777-74-4, **Protein** L 29 (Saccharomyces cerevisiae ribosome gene CYH2) 92354-93-3, **Protein** 29 (Saccharomyces cerevisiae ribosome) 94046-97-6, **Protein** L 16 (Saccharomyces uvarum ribosome) 95917-58-1, **Protein** L 46 (yeast ribosome) 98616-24-1, **Protein** S 10 (Saccharomyces uvarum clone TJP113 ribosome) 110639-11-7, Ubiquitin (Saccharomyces cerevisiae gene UBI1 precursor reduced) 110639-12-8, Ubiquitin (Saccharomyces cerevisiae gene UBI3 precursor reduced) 125360-57-8, **Protein** GRP 78 (Saccharomyces cerevisiae clone pK11 precursor) 125524-15-4, **Protein** (Saccharomyces cerevisiae gene SAR1) 125752-38-7, **Protein** hsp 26 (Saccharomyces cerevisiae) 128875-87-6, **Protein** (Saccharomyces cerevisiae clone pME21 gene MER1 reduced) 130453-59-7 131201-81-5, **Proteinase** (Saccharomyces cerevisiae clone 8 YC7.alpha.-subunit reduced) 131463-43-9, **Protein** hsp 12 (Saccharomyces cerevisiae strain S288C) 135541-78-5 136253-29-7, **Protein** (Saccharomyces cerevisiae clone pUC18-84 gene MFT1) 139021-13-9, **Protein** (Saccharomyces cerevisiae clone pRB543 158-**amino acid** reduced) 144198-49-2, **Protein** L 9 (Saccharomyces cerevisiae gene YL9A ribosome) 145185-46-2, **Protein** L 41a (Saccharomyces cerevisiae strain AH22 ribosome reduced) 146213-06-1, **Protein** (Saccharomyces cerevisiae clone G4B 309-**amino acid** reduced) 146213-72-1,

Protein (Saccharomyces cerevisiae clone 5239 483-**amino acid**) 146213-82-3, **Protein** (Saccharomyces cerevisiae clone 5307 136-**amino acid** reduced) 146213-96-9, **Protein** (Saccharomyces cerevisiae clone 6589 315-**amino acid** reduced) 147154-16-3 147258-86-4 148024-84-4, Transcription factor S-II (Saccharomyces cerevisiae clone pYSII-2 gene PRP2 reduced) 148266-06-2, **Protein** FKBP 13 (Saccharomyces cerevisiae clone Y13-8A gene FKB2 precursor reduced) 148710-69-4, Zuotin (Saccharomyces cerevisiae clone pETZUO1 gene ZUO1) 149023-10-9
150790-09-3 151879-01-5 156987-01-8 157884-81-6 157910-28-6
158652-22-3 158889-52-2 158889-55-5 162570-32-3 162570-64-1
163481-21-8 164205-50-9 167942-63-4 167942-70-3 169240-61-3
169538-96-9 170085-27-5 170907-24-1 171344-26-6 175645-88-2
175674-35-8 176522-07-9 176671-10-6 177257-28-2 177700-24-2
179096-09-4 182513-92-4 182577-86-2 183564-23-0 184922-90-5
187415-07-2 189259-78-7, **Protein** (Saccharomyces cerevisiae gene YOL031C) 190857-63-7 191747-24-7 196218-31-2 207807-86-1
222535-66-2 245113-90-0 245113-94-4 259240-52-3 309765-51-3
320426-39-9 320426-40-2 320426-41-3 320426-42-4 320426-43-5
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320427-94-9 320427-95-0 320427-96-1 320427-97-2 320427-98-3
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320428-09-9 320428-10-2 320428-11-3 320428-12-4 320428-13-5
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320428-19-1 320428-20-4 320428-21-5 320428-22-6 320428-23-7
320714-27-0 320714-28-1 320714-30-5
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**amino acid** sequence; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT 128981-79-3
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene YDL133C-A **protein**; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT 318254-83-0

RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene YDL133CA **protein**; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT 320714-29-2
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene YJL188C **protein**; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

IT 204662-85-1 318450-36-1 318450-37-2 318450-38-3 318450-39-4
318450-40-7 318450-41-8 318450-42-9 318450-43-0 318450-44-1
318450-45-2 318450-46-3 318450-47-4 318450-48-5 318450-49-6
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318450-66-7 318450-67-8 318450-68-9 318450-69-0 318450-70-3
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318450-87-2 318450-89-4 318450-90-7 318450-91-8 318450-92-9
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320426-93-5 320426-97-9 320427-08-5 320427-11-0 320427-14-3
320427-22-3 320427-26-7 320427-30-3 320427-44-9 320427-51-8
320427-55-2
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug

screening and vaccines)

IT 320427-70-1 320427-72-3 320427-77-8 320427-81-4 320427-85-8
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; **apoptosis**-related genes and **protein** in yeast and **fungi** and their use in drug **screening** and vaccines)

L83 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:176262** HCAPLUS
DN **133:27198**
TI Isolation of **peptide** aptamers that inhibit intracellular processes
AU Blum, Jonathan H.; Dove, Simon L.; Hochschild, Ann; Mekalanos, John J.
CS Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, MA, 02115, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**2000**), 97(5), 2241-2246
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): **1**, 10
AB We have developed a method for isolation of random **peptides** that inhibit intracellular processes in **bacteria**. A library of random **peptides** expressed as fusions to Escherichia coli thioredoxin (aptamers) were expressed under the tight control of the arabinose-inducible PBAD promoter. A selection was applied to the library to isolate aptamers that interfered with the activity of thymidylate synthase (ThyA) in vivo. Expression of an aptamer isolated by this method resulted in a ThyA- phenotype that was suppressed by simultaneous overexpression of ThyA. Two-hybrid anal. showed that this aptamer is likely to interact with ThyA in vivo. The library also was **screened** for aptamers that inhibited growth of **bacteria** expressing them, and five such aptamers were characterized. Four aptamers were **bacteriostatic** when expressed, whereas one showed a **bactericidal** effect. Introduction of translational stop codons into various aptamers blocked their activity, suggesting that their biol. effects were likely to be due to **protein** aptamer rather than RNA. Combinatorial aptamers provide a new genetic and biochem. tool for identifying targets for **antibacterial** drug development.
ST aptamer based **bacterial** inhibition system; ABBIS **peptide** aptamer **bacteria** growth inhibition
IT **Drug screening**
(ABBIS (aptamer-based **bacterial** inhibition systems)-based; isolation of **peptide** aptamers that inhibit intracellular processes)
IT **Peptide** library
(aptamer, ABBIS; isolation of **peptide** aptamers that inhibit intracellular processes)
IT Thioredoxins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aptamers, fusion **protein** moiety; isolation of **peptide** aptamers that inhibit intracellular processes)
IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aptamers; isolation of **peptide** aptamers that inhibit intracellular processes)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(araBAD; isolation of **peptide** aptamers that inhibit intracellular processes)
IT Escherichia coli
(as expression host; isolation of **peptide** aptamers that inhibit intracellular processes)
IT **Cell death**
(**bacterial**, aptamer-induced; isolation of **peptide** aptamers that inhibit intracellular processes)
IT Growth, **microbial**
(inhibition, by aptamers; isolation of **peptide** aptamers that inhibit intracellular processes)
IT **Bacteria** (**Eubacteria**)
Plasmid vectors
(isolation of **peptide** aptamers that inhibit intracellular processes)
IT **Antimicrobial agents**
(**peptide** aptamers as, **screening** of; isolation of **peptide** aptamers that inhibit intracellular processes)
IT 9031-61-2, Thymidylate synthase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition, by aptamers; isolation of **peptide** aptamers that inhibit intracellular processes)
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L83 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:753388** HCAPLUS
DN **132:1799**
TI Compounds, **screening** methods, and uses involving anti-**apoptotic** genes and gene products
IN Goldmakher, Viktor S.; Skaletskaya, Anna; Bartle, Laura
PA Apoptosis Technology, Inc., USA
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-70
ICS C12Q001-68; A61K031-70; A61K039-42; C07K014-045; C07H021-04
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 3, **64**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9960171	A1	19991125	WO 1999-US6567	19990506	<--
	W: AU, CA, JP, NZ					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 6218511	B1	20010417	US 1998-80265	19980518	<--
	CA 2329868	AA	19991125	CA 1999-2329868	19990506	<--
	AU 9939643	A1	19991206	AU 1999-39643	19990506	<--
	EP 1080233	A1	20010307	EP 1999-922704	19990506	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2002515267	T2	20020528	JP 2000-549777	19990506	<--
PRAI	US 1998-80265	A	19980518	<--		
	US 1999-301121	A	19990428	<--		
	WO 1999-US6567	W	19990506	<--		

AB Novel **polypeptides** having anti-**apoptotic** activity, and methods of **screening** for such novel **polypeptides** and polynucleotides encoding such **polypeptides** having anti-**apoptotic** activity are provided. Methods of **screening** for compds. that regulate or modulate **apoptosis** and/or anti-**apoptotic** activity, such as compds. that induce, restore, or modulate **apoptosis** and/or inhibit, diminish, or modulate anti-**apoptotic** activity are also provided. Such **screening** methods are generally based on binding of agents to a **death** receptor such as Fas receptor or tumor necrosis factor receptor I, or activation of a signal transduction pathway for **apoptosis**. UL37 and its isoforms from human **cytomegalovirus** is identified as an anti-**apoptotic** activity, and thus may be used in methods of **screening** for and identifying physiol. mols. that specifically binding to at least of of the isoforms in an in vitro binding assay. Examples of such physiol. mols. are FADD, FLICE, caspase 3, Apaf-1, Bcl-xL, Bcl-2, Bak, ICE, Bax, and BNIP-3. Methods of using such compds. in the therapeutic treatment of diseases and methods of treating eukaryotic **cells** with compds. that regulate or modulate **apoptosis** and/or anti-**apoptotic** activity are described, as well as methods of enhancing the stability, growth, and/or productivity of eukaryotic **cells** and pharmaceutical compns. that regulate or modulate **apoptosis** and/or anti-**apoptotic** activity. A preferred embodiment is a method of identifying **antiviral** compds. that specifically binding to human **cytomegalovirus**

polypeptides having anti-**apoptotic** activity or modified forms of such **polypeptides**.

ST **apoptosis** inhibiting gene **protein screening**; human **cytomegalovirus antiapoptosis protein** UL37; **antiviral screening apoptosis** inhibitor **cytomegalovirus**

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Apaf-1; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(BNIP-3; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Bax; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Bcl-x; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(FADD; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **USES (Uses)**
(UL37; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Autoimmune disease
Infection
Neoplasm
(aberrant **apoptotic** activity in; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Phosphorothioate oligonucleotides
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(antisense; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Gene, animal
Gene, **microbial**
Proteins, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **USES (Uses)**
(**apoptosis**-inhibiting; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT **Proteins**, specific or class
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse);

BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(bcl-2; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Nervous system
(central, gene therapy by transfection or **retroviral** infection of embryonic; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Animal **virus**
Antiviral agents
Apoptosis
Drug screening
Gene therapy
Human **herpesvirus** 5
Retroviral vectors
Virus vectors
(compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Antisense DNA
Antisense RNA
Antisense oligonucleotides
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Cardiovascular system
(disease, aberrant **apoptotic** activity in; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Immunity
(disorder, aberrant **apoptotic** activity in; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Transformation, genetic
(double transformation assay; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Fibroblast
Hematopoietic precursor cell
Hybridoma
Lymphocyte
(gene therapy by transfection or **retroviral** infection; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Microprojectile bombardment
(gene therapy with; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Heart, disease
(infarction, aberrant **apoptotic** activity in; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Drug delivery systems
(liposomes; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)

IT Tumor necrosis factor receptors
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(p55, **screening** for agents binding to; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
IT Fas antigen
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(**screening** for agents binding to; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
IT Signal transduction, biological
(**screening** for agents modulating; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
IT Adeno-associated **virus**
Adenoviridae
Avipoxvirus
Baculoviridae
Human **herpesvirus**
Vaccinia **virus**
(vectors; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
IT Infection
(**viral**, aberrant **apoptotic** activity in; compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
IT 122191-40-6, ICE **proteinase** 169592-56-7, Caspase 3
179241-78-2, FLICE protease
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(compds., **screening** methods, and uses involving anti-**apoptotic** genes and gene products)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Colberg-Poley, A; Journal of Virology 1992, V66(1), P95 HCAPLUS
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L83 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:704891** HCAPLUS
DN **131:307087**
TI **Screening** methods for the identification of compounds that modulate **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by an immunodeficiency **virus**
IN Finkel, Terri H.; Casella, Carolyn
PA National Jewish Medical and Research Center, USA
SO U.S., 12 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12Q001-70
NCL 435005000
CC 1-5 (**Pharmacology**)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 5976786 A 19991102 US 1996-774269 19961227 <--
US 2002091073 A1 20020711 US 2001-881573 20010613 <--
PRAI US 1995-9460P P 19951229 <--
US 1996-774269 A1 19961227 <--
US 1999-389944 B1 19990903 <--

AB Disclosed is a method to limit infection by an immunodeficiency **virus**. The method includes inhibiting an immunodeficiency **virus protein** which regulates **apoptosis** in cells. Also disclosed are methods to identify compds. that regulate cellular inhibitors of **apoptosis** in cells infected with an immunodeficiency **virus** and compds. identified thereby.

ST immunodeficiency **virus** cell **apoptosis** drug **screening**

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cleavage; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT Chromatin
(condensation; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT Gene
(expression; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene vpr; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT Membrane, biological
(membrane permeability; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT Gene, **microbial**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nef; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT Biological transport
(permeation, membrane permeability; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT **Antiviral agents**
Apoptosis
CD4-positive T cell
Drug screening
Human immunodeficiency **virus**
Human immunodeficiency **virus** 1
Organelle
Protein degradation
Simian immunodeficiency **virus**
Transcription, genetic
Translation, genetic
(**screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)

IT **Viral** RNA

nef **protein**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)
IT Gene, **microbial**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vpr; **screening** for compds. modulating **apoptosis** in immunodeficiency **virus**-infected cells, and method to limit infection by immunodeficiency **virus**)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 9421806 1994 HCAPLUS
(2) Balotta; J of Virol 1993, V67(7), P4409 HCAPLUS
(3) Finkel; Curr Opin Immunol 1994, V6, P605 MEDLINE
(4) Finkel; Current Opinion in Immunol 1994, V6, P605 MEDLINE
(5) Finkel; Nature Med 1995, V1, P129 HCAPLUS
(6) Hattori; Proc Natl Acad Sci 1990, V87, P8080 HCAPLUS
(7) Ho; Nature 1995, V373, P123 HCAPLUS
(8) Lang; J of Virol 1993, V67(2), P902 HCAPLUS
(9) Levy; Cell 1993, V72, P541 HCAPLUS
(10) Ogawa; J of Virol 1989, V63(9), P4110 HCAPLUS
(11) Pantaleo; Nature Med 1995, V1, P118 HCAPLUS
(12) Pantaleo; Nature Med 1995, V1, P118 HCAPLUS
(13) Rogel; J of Virol 1995, V69, P882 HCAPLUS
(14) Shibata; J of Virol 1990, V64(2), P742 HCAPLUS
(15) Xiping; Nature 1995, V373, P117

L83 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:614168** HCAPLUS
DN **131:223475**
TI **Screening** for substances with an anti-HIV action
IN Weber, Olaf; Hug, Hubert
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C12Q001-00
CC 1-1 (**Pharmacology**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9947696	A2	19990923	WO 1999-EP1512	19990309 <--
	WO 9947696	A3	20000420		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19812181	A1	19990923	DE 1998-19812181	19980319 <--
	AU 9931444	A1	19991011	AU 1999-31444	19990309 <--
	EP 1064546	A2	20010103	EP 1999-913246	19990309 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002506983	T2	20020305	JP 2000-536879	19990309 <--
PRAI	DE 1998-19812181	A	19980319 <--		

WO 1999-EP1512 W 19990309 <--

AB The invention relates to new assays for detecting substances influencing **apoptosis** for a new treatment of the disease caused by the human immunodeficiency **virus** (HIV). The invention is based on the discovery in the human immunodeficiency **virus** (HIV) of a new region homologous to the "**death** effector domain" (DED) and on a new **antiviral** strategy, based on said discovery, for eliminating HIV-infected **cells** from the body and preventing the acquired immune deficiency syndrome (AIDS).

ST AIDS **apoptosis** HIV death effector domain

IT **Protein** motifs
(death-effector domain; **screening** for substances with an anti-HIV action)

IT AIDS (disease)
Antiviral agents
Apoptosis
Drug screening
Human immunodeficiency **virus**
Human immunodeficiency **virus** 1
Transformation, genetic
(**screening** for substances with an anti-HIV action)

IT Fas antigen
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(**screening** for substances with an anti-HIV action)

IT 243868-56-6
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**screening** for substances with an anti-HIV action)

L83 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2003 ACS

AN **1999:375704** HCAPLUS

DN **131:14859**

TI Method for determining gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes with a vector containing antisense polynucleotide sequences and an inducible gene control region

IN Marra, Andrea; Rosenberg, Martin; Ji, Yinduo

PA SmithkKine Beecham Corporation, USA

SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C12Q001-68
ICS C12N015-64; C12N015-74; C12N015-75; C12N015-76; C12N015-77; C12N015-78; C12N015-79; C12N015-81; C12N015-85; C07H021-02; C07H021-04

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 10

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9928508	A1	19990610	WO 1998-US25808	19981204
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1034308	A1	20000913	EP 1998-962914	19981204
	R: BE, CH, DE, DK, FR, GB, IT, LI, NL				
	JP 2002503447	T2	20020205	JP 2000-523383	19981204
PRAI	US 1997-67446P	P	19971204		
	US 1998-82534P	P	19980420		
	US 1998-105161P	P	19981021		

WO 1998-US25808 W 19981204

AB The present invention provides a mol. genetic method for detg. gene essentiality and is comprised of: (1) transforming a host **cell** with a vector (or library) that has an inducible gene control region expressibly linked to random polynucleotides or antisense polynucleotides, (2) inducing said inducible gene control region with an inducer and (3) detecting an alteration in the metab. and/or **death** or slowed growth of the host **cell**. The inducible gene control region is an inducible promoter or an operator and inducible repressor. The inducer may be a chem. compd. (such as iso-Pr .beta.-thiogalactopyranoside (IPTG), doxycycline, erythromycin, or tetracycline) or may be electromagnetic radiation (such as UV light, visible light, red visible light, or green visible light). The invention specifically presented the construction of plasmid vectors pYJ318-7 and pYJ318-16, which contain antisense hla and sense hla sequences resp., and used these plasmids in transforming Staphylococcus aureus. The invention also characterized the S. aureus transformants. Plasmid vectors pYJ318-7 and pYJ318-16 contained gene tetR/tetR promoter/xyl-tet promoter-operator fusion/gene hla (antisense or sense)/gene cat. This tet regulatory expression system in transformed S. aureus was confirmed using tetracycline, and the data showed that tet regulatory system can efficiently regulate expression of genes downstream of the xyl/tet promoter operator fusion in S. aureus. The data also showed that hla antisense RNA can be specifically induced by tetracycline using the tet regulatory system in S. aureus. The antisense strategy described in this invention can be used for creating libraries of conditionally expressed and conditional lethal mutant **bacteria**. The invention also eluded to the use of this method as a powerful approach for studying mol. **pathogenesis** and for detg. mol. targets for antibiotic discovery.

ST method detg gene essentiality transformation antisense polynucleotide inducible promoter; antisense polynucleotide inducible promoter vector prokaryote transformation gene essentiality

IT Metabolism, **microbial**
(alteration; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Polynucleotides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(antisense; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Reporter gene
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(cat; construction of a tet regulatory system (plasmids pYJ318-7 and pYJ318-16) and use in regulating the expression of genes downstream of promoter)

IT Gene, **microbial**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(detg. gene essentiality; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Eukaryote (Eukaryotae)
(filamentous; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Light

(green, promoter inducer, visible; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Streptococcus
(group C; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Streptococcus
(group D; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Streptococcus
(group G; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Promoter (genetic element)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(inducible, tetR and xyl-tet hybrid promoters; method for detg. gene essentiality, transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT **Acinetobacter**
Actinobacillus
Actinomyces
Actinomyces israelii
Aeromonas
Archaebacteria (Archaea)
Bacillus (**bacterium** genus)
Bacillus anthracis
Bacillus cereus
Bordetella
Bordetella bronchiseptica
Bordetella parapertussis
Bordetella pertussis
Borrelia
Brucella
Brucella melitensis
Calymmatobacterium
Campylobacter
Candida
Candida albicans
Cell death
Chlamydia
Chlamydia trachomatis
Citrobacter freundii
Clostridium
Clostridium botulinum
Clostridium perfringens
Clostridium tetani
Corynebacterium
Corynebacterium diphtheriae
Enterobacter
Enterococcus durans
Enterococcus faecalis
Enterococcus faecium
Erwinia
Erysipelothrix
Escherichia

Escherichia coli
Francisella
Francisella tularensis
Gardnerella vaginalis
Haemophilus
Haemophilus ducreyi
Haemophilus influenzae
Haemophilus influenzae aegyptius
Haemophilus parainfluenzae
Klebsiella
Klebsiella pneumoniae
Kluyveromyces
Kluyveromyces lactis
Legionella
Leptospira
Listeria
Listeria monocytogenes
Moraxella
Mycobacterium
Mycobacterium bovis
Mycobacterium leprae
Mycobacterium tuberculosis
Mycobacterium ulcerans
Mycoplasma
Neisseria
Neisseria gonorrhoeae
Neisseria meningitidis
Nocardia
Pasteurella
Prokaryote
Proteus (**bacterium**)
Proteus mirabilis
Proteus vulgaris
Pseudomonas
Pseudomonas aeruginosa
Rickettsia
Rickettsia rickettsi
Saccharomyces
Saccharomyces cerevisiae
Salmonella
Salmonella typhi
Serratia marcescens
Serratia proteamaculans proteamaculans
Shigella
Shigella dysenteriae
Shigella flexneri
Spirillum
Staphylococcus
Staphylococcus aureus
Staphylococcus epidermidis
Streptobacillus
Streptococcus
Streptococcus agalactiae
Streptococcus group A
Streptococcus group B
Streptococcus pneumoniae
Streptococcus pyogenes
Streptomycetes
Transformation, genetic
Treponema
Treponema pallidum
Vibrio
Vibrio cholerae

Yersinia
Yersinia pestis
(method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Antisense oligonucleotides
Enhancer (genetic element)
Polynucleotides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Genetic element
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(operator, inducible, xyl-tet promoter-operator fusion; method for detg. gene essentiality, transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Plasmid vectors
(pYJ318-7 (antisense hla) and pYJ318-16 (sense hla); construction of a tet regulatory system (plasmids pYJ318-7 and pYJ318-16) and use in regulating the expression of genes downstream of promoter)

IT Electromagnetic wave
Light
UV radiation
(promoter inducer; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Light
(red, promoter inducer, visible; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Growth, **microbial**
(slowed; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(terminator; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT Eukaryote (Eukaryotae)
(unicellular; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

IT **60-54-8**, Tetracycline 114-07-8, Erythromycin 367-93-1, IPTG **564-25-0**, Doxycycline
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(promoter inducer; method for detg. gene essentiality, genetic transformation of prokaryotes and/or unicellular eukaryotes using a vector contg. antisense polynucleotide sequences and an inducible gene control region)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Mirabelli; US 5639595 A 1997 HCAPLUS

L83 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:8208 HCAPLUS
DN 130:61060
TI Inhibition of the Src kinase family pathway as a method of treating hepatitis B **virus** infection and hepatocellular carcinoma
IN Schneider, Robert J.; Klein, Nicola
PA New York University Medical Center, USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-53
ICS C12Q001-70; C07H021-04; A61K048-00; A61K038-00
CC 1-5 (**Pharmacology**)
Section cross-reference(s): 3, 9, 10, 14, **63**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9857175	A1	19981217	WO 1998-US12279	19980612 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6420338	B1	20020716	US 1997-874430	19970613 <--
	AU 9878385	A1	19981230	AU 1998-78385	19980612 <--
	EP 988548	A1	20000329	EP 1998-926584	19980612 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2003032596	A1	20030213	US 2002-196344	20020715 <--
PRAI	US 1997-874430	A	19970613 <--		
	WO 1998-US12279	W	19980612 <--		

AB The present invention relates to therapeutic protocols and pharmaceutical compns. designed to target HBx **protein**-mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of hepatitis B **virus** (HBV) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of HBV infection targeted to HBx and its essential activities required to sustain HBV replication. The invention is based, in part, on the discovery that activation of Src kinase signaling cascades plays a fundamental role in mammalian **hepadnavirus** replication. HBx mediates activation of the Src family of kinases and this activation is a crit. function provided by HBx for mammalian **hepadnavirus** replication.
ST Src kinase hepatitis B **virus** inhibition; **antiviral** hepatitis B inhibition HBx **protein**; hepatocellular carcinoma treatment Src kinase HBV inhibition
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator **protein** 1), HBx **protein** transactivation of, through Src kinases activation; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)
IT Animal cell line
(Chang liver, Src kinases and HBx **protein** expression in; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)
IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU

(Therapeutic use); BIOL (Biological study); PROC (Process); **USES (Uses)**
(Csk, inhibiting kinase activity of Src kinase; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Quaternary structure
(DNA triplex, compd. forming, to block transcription of Src kinase gene; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(HBx (hepatitis B **virus**, X), as intracellular activator of Src kinase; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Animal cell line
(Hep G2, Src kinases and HBx **protein** expression in; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MAP kinase kinase, compd. inhibiting or interfering with activity of; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MAP kinase, compd. inhibiting or interfering with activity of; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Myc, compd. inhibiting or interfering with activity of; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Woodchuck hepatitis B **virus**
(Src family kinases in in vitro replication of; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(WHx, Src family kinases in relation to; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Cell death**
(agent inducing, in **antiviral** agent **screening**; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Antisense oligonucleotides
Ribozymes
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(blocking translation of Src kinase gene; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, general, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cellular or **viral**, compds. interfering with Src kinase

interaction with; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Ras **proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compd. inhibiting or interfering with activity of; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Plasmids
(expressing wild-type or mutated HBx mRNA; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(for Src kinase; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); **USES (Uses)**
(gene HcK, dominant-neg. mutant of, interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene N-myc, HBx **protein** induction of, through Src kinases activation; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); **USES (Uses)**
(gene Yes, dominant-neg. mutant of, interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Phosphoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gene fyn, dominant-neg. mutant of, interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Liver, neoplasm
(hepatoma; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Immunoassay
(in **antiviral** agent **screening**; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in **antiviral** agent **screening**; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Yeast**
(inducibly expressing Src kinase gene, for **antiviral** agent **screening**; inhibition of Src kinase family pathway in treatment

of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Antiviral agents**
Drug delivery systems
Drug screening
Hepatitis B **virus**
Signal transduction, biological
(inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monoclonal, to Ras **protein**; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Gene, **microbial**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of HBV, in **antiviral** agent **screening**; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Translation, genetic
(of Src kinase gene, antisense or ribozyme mol. blocking; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Transcription, genetic
(of Src kinase gene, triple helix-forming compd. blocking; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT **Phosphopeptides**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(phosphotyrosine-contg., interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT DNA formation
(replication, **viral**, compd. modulating HBx **protein** activities required for; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Human **adenovirus**
(replication-defective recombinant, expressing wild-type or mutated HBx mRNA; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(to Src kinase family; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT Cytotoxic agents
(tyrphostins, inhibitor derived from, inhibiting kinase activity of Src kinase; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT 155215-87-5, JNK kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HBx **protein** activation of, through Src kinases activation; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT 271-80-7D, 1H-Pyrazolo[3,4-d]pyrimidine, derivs., salts 2700-22-3D, derivs., salts 152478-16-5, Angelmicin 152478-16-5D, Angelmicin, pharmaceutically-acceptable salts
RL: BPR (Biological process); BSU (Biological study, unclassified); THU

(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibiting kinase activity of Src kinase; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT 141349-89-5P, Src kinase 141349-89-5P
RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT 141349-89-5D, Src kinase, dominant-neg. mutants
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

IT 21820-51-9, Phosphotyrosine
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**peptide** contg., interfering with Src kinase **protein** interactions; inhibition of Src kinase family pathway in treatment of hepatitis B **virus** infection and hepatocellular carcinoma)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bennett, W; Proc Annu Meet Am Assoc Canc Res 1995, V36, P699
(2) Hofschneider, P; Cancer Weekly Plus 1996
(3) Klein, N; Dissertation Abstracts International 1997, V58(4B), P1696
(4) Li, P; Anticancer Research 1993, V13(6A), P1957 HCAPLUS
(5) Uehara, Y; Journal of Antibiotics 1993, V46(8), P1306 HCAPLUS
(6) Yamaguchi, M; Leukemia 1997, V11, P497 HCAPLUS

L83 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2003 ACS

AN **1997:267275** HCAPLUS

DN **126:248580**

TI **Screening** methods for the identification of inducers and inhibitors of programmed **cell death** (**apoptosis**)

IN Roizman, Bernard; Chou, Joany

PA Arch Development Corporation, USA

SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-50
ICS G01N033-68

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 13

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9709617	A1	19970313	WO 1996-US14125	19960829
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5834216	A	19981110	US 1995-524344	19950906
CA 2230988	AA	19970313	CA 1996-2230988	19960829
AU 9669123	A1	19970327	AU 1996-69123	19960829
EP 874986	A1	19981104	EP 1996-929881	19960829
EP 874986	B1	20011107		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

	JP 11512517	T2	19991026	JP 1996-511336	19960829
	AT 208496	E	20011115	AT 1996-929881	19960829
	ES 2164915	T3	20020301	ES 1996-929881	19960829
PRAI	US 1995-524344	A	19950906		
	WO 1996-US14125	W	19960829		

AB The method exploits the finding that the exposure of cells to **apoptotic** stress and its concurrent shutdown of cellular **protein** synthesis is accompanied by phosphorylation of eIF-2.alpha. and a novel **protein** termed p90. For **screening** candidate inhibitors of **apoptosis**, the method comprises: (1) prepg. duplicate human cell cultures; (2) exposing one of the duplicate cell cultures to a candidate inhibitor; (3) exposing the duplicate cell cultures to an **apoptotic** stress, e.g., by infection with a herpes simplex **virus**; (4) prepg. resp. cell lysates from the duplicate cell cultures of step 3; (5) contacting the lysates of step 4 with ATP wherein the .gamma.-phosphate of ATP has a detectable label, e.g., 32P; and (6) measuring the levels of phosphorylated p90 and/or eIF-2.alpha. produced by the lysates, whereby inhibitors of **apoptosis** are identified by their ability to prevent or decrease phosphorylation of eIF-2.alpha. and/or p90 when compared to the level of phosphorylation of eIF-2.alpha. and/or p90 in cells not exposed to the candidate substance. Details of the method for **screening** candidate inducers are given also.

ST **apoptosis** inducer inhibitor **screening protein** phosphorylation; eIF2alpha phosphorylation **apoptosis** inducer inhibitor **screening**; p90 phosphorylation **apoptosis** inducer inhibitor **screening**

IT Animal cell line
(SK-N-SH; **screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT Animal cell line
(**Vero**; **screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT Initiation factors (**protein** formation)
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(eIF-2; .alpha.-, **screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(p90; **screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT Animal tissue culture
Apoptosis
Cosmids
Fibroblast
Genetic vectors
HeLa cell
Human **herpesvirus** 1
Phosphorylation, biological
Plasmids
Translation, genetic
(**screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT **Phosphoproteins**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

IT 2964-07-0, ATP-.gamma.-32P

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)
IT 82249-72-7, EIF-2.alpha. kinase 182372-19-6, **Protein** kinase PKR
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**screening** for **apoptosis** inducers and inhibitors by detecting **protein** phosphorylation)

=> fil wpix
FILE 'WPIX' ENTERED AT 13:40:48 ON 06 MAY 2003
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FILE LAST UPDATED: 5 MAY 2003 <20030505/UP>
MOST RECENT DERWENT UPDATE: 200329 <200329/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

Due to data production problems in updates 24 and 25 the WPI file had to be reset to update 200323 on April 24 and the corrected updates were reloaded. SDIs for update 24 were rerun. The previous SDI run for 24 has been credited. We also recommend to recreate answer sets dated between April 10 and 24. Charges incurred to accomplish this will be credited of course.

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> SLART (Simultaneous Left and Right Truncation) is now available in the /ABEX field. An additional search field /BIX is also provided which comprises both /BI and /ABEX <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech abex tot

L110 ANSWER 1 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2003-058503** [05] WPIX
DNC **C2003-014998**
TI Novel isolated programmed **cell death**-related **polypeptide**, NARC10 and NARC16, useful for treating disorders associated with abnormal apoptotic process e.g. Alzheimer's disease, cancer, myocardial infarction, stroke.
DC B04 D16
IN CHIANG, L W
PA (MILL-N) MILLENNIUM PHARM INC
CYC 99
PI WO 2002081516 A2 20021017 (200305)* EN 123p C07K014-47
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW

ADT WO 2002081516 A2 WO 2002-US1098 20020116

PRAI US 2002-47855 20020115; US 2001-262306P 20010116

IC ICM C07K014-47

AB WO 200281516 A UPAB: 20030121

NOVELTY - An isolated **polypeptide** (I) comprising an amino acid sequence of:

(a) a fragment of fully defined programmed **cell death**-related **polypeptide** sequence of 182 (S1) or 672 (S2) amino acids; or

(b) a variant of (S1) or (S2), is new.

DETAILED DESCRIPTION - An isolated **polypeptide** (I) comprising an amino acid sequence of:

(a) fragment comprising at least 15 contiguous amino acids of fully defined programmed **cell death**-related **polypeptide** sequence of 182 (S1) or 672 (S2) amino acids as given in the specification;

(b) variant of (S1) or (S2) which is encoded by a nucleic acid molecule that hybridizes to the complement of a fully defined programmed **cell death**-related polynucleotide sequence of 2034 (S3) or 3206 (S4) nucleotides as defined in the specification;

(c) variant of S1 or S2 which is encoded by nucleotides sequence having 70% sequence identity with (S3) or (S4), respectively. (S1) is the fully defined NARC10 **polypeptide** sequence, and (S2) is the fully defined NARC16 **polypeptide** sequence.

INDEPENDENT CLAIMS are also included for:

(1) an isolated nucleic acid molecule (II) comprising a nucleotide sequence:

(a) having at least 70% sequence identity with (S3) or (S4);

(b) consisting of at least 20 contiguous nucleotides of (S3) or (S4);

(c) encoding (S1) or (S2);

(d) encoding a fragment which consists of 15 contiguous amino acids of (S1) or (S2;

(e) encoding a variant of (S1) or (S2) that hybridizes to (S3) or (S4) under stringent conditions; or

(f) complementary to the above sequences;

(2) a host **cell** (III) which contains (II);

(3) an antibody (IV) which selectively binds to (I);

(4) preparation (M1) of (I);

(5) detecting (M2) presence of (II) in a sample involves contacting the sample with a nucleic acid probe which hybridizes to the nucleic acid molecule and determining whether the nucleic acid probe binds to the nucleic acid molecule in the sample;

(6) a kit (V) comprising a compound which selectively binds to (I) or selectively hybridizes to (II), and instructions for use; and

(7) modulating (M3) the activity of (I) involves contacting the **polypeptide** or a **cell** expressing a **polypeptide** with a compound which binds to the **polypeptide** to modulate the activity of the **polypeptide**.

ACTIVITY - Cytostatic; Immunosuppressive; Dermatological; Antiinflammatory; Nephrotropic; Anti-HIV; Nootropic; Neuroprotective; Antianemic; Cardiant; Cerebroprotective; Vasotropic; Antidiabetic; Immunosuppressive; Thyromimetic; Immunostimulant; Anticonvulsant; Antimanic; Tranquilizer; Hypotensive; Neuroleptic.

No biological data given.

MECHANISM OF ACTION - Activity or expression of NARC10 or NARC16 protein or nucleic acid modulator; Gene therapy.

USE - (I) is useful for identifying a compound which binds to it or modulates its activity. (III) is useful for preparing (I) by recombinant techniques. (IV) is useful for detecting the presence of (I) in a sample

(claimed). (II) is useful for identifying a compound that modulates the expression of programmed **cell death**-related genes.
Fragments of (II) are useful as primers or probes for detecting programmed **cell death** protein like-encoding nucleic acids. The probes are useful for detecting transcripts or genomic sequences encoding the same or identical proteins, as part of a diagnostic test kit for identifying **cells** or tissues that misexpress programmed **cell death**-related **polypeptide**, etc. (II) is useful for expressing (I) via a recombinant expression vector in a host **cell** in gene therapy applications, to detect NARC10 or NARC16 mRNA, or genetic alteration in NARC10 or NARC16 gene and to modulate NARC10 or NARC16 activity. Fragments of (II) are useful as probes and primers.

Portions or fragments of (II) are useful to:

(a) map their respective genes on a chromosome, e.g. to locate gene regions associated with genetic disease or to associate NARC10 or NARC16 with a disease;

(b) identify an individual from a minute biological sample (tissue typing); and

(c) aid in forensic identification of a biological sample.

(I) and (IV) are useful for modulating the apoptotic process, and thus useful for modulating, and treating disorders associated with increased apoptosis, inhibition of apoptosis or disruptions in cell cycle. Preferably, (I) and (IV) are useful for treating disorders associated with abnormally low rate of apoptosis, e.g. cancers including follicular lymphomas, carcinomas with p53 mutations, or hormone-dependent tumors, autoimmune disorders including systemic lupus erythematosus, diabetes, graft rejection, Hashimoto's thyroiditis and immune-mediated glomerulonephritis; and viral infections e.g. infections caused by herpes viruses.

(I), (II), (M1) and (IV) are useful for treating disorders associated with increased rate of apoptosis e.g. virus-induced lymphocyte depletion (including acquired immunodeficiency syndrome (AIDS)), neurodegenerative diseases manifested by loss of specific sets of neurons (including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, spinal muscular atrophy, retinitis pigmentosa, and cerebellar degeneration), myelodysplastic syndromes (including aplastic anemia), ischemic injuries (including myocardial infarction, stroke and reperfusion injury), and toxin (e.g. alcohol) induced liver disease. (I) and (IV) are also useful for treating excessive apoptotic conditions associated with:

(a) heart tissue e.g. idiopathic dilated cardiomyopathy, ischemic cardiomyopathy, and valvular heart disease; and

(b) production of blood cells e.g. aplastic anemia, chronic neutropenia, and myelodysplastic syndromes.

(I) and (IV) are also useful for treating central nervous system disorders e.g. senile dementia, Huntington's disease, hypertension, schizophrenia, attention deficit disorder, mania, anxiety, severe bipolar affective disorder (BP-I). (IV) is useful for regulating cellular functions including programmed cell death, nucleosome assembly, phosphate homeostasis and cell cycle. (I), (II) and (IV) are useful for:

(a) screening assays;

(b) detection assays (chromosomal mapping, tissue typing, forensic biology);

(c) predictive medicine (e.g. diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenetics); and

(d) methods of treatment (e.g. therapeutic and prophylactic).

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-C01G; B04-E02F; B04-E05; B04-F0100E; B04-N04A0E; B11-C07A; B11-C08E5; B11-C08F2; B11-C10; **B12-K04A**; **B12-K04E**; **B12-K04F**; B14-A02; B14-A02A3; B14-F01; B14-F01E; B14-F02; B14-F02D1; B14-F03; B14-F05; B14-G01B; B14-G02C; B14-G02D; B14-H01;

B14-J01A3; B14-J01A4; B14-J01B3; B14-J01B4; B14-L01; B14-L06; B14-N03; B14-N10; B14-N11; B14-N12; B14-N16; B14-S01; B14-S03; B14-S04; D05-C11; **D05-H09**; D05-H11; D05-H12A; D05-H12D1; D05-H12E; D05-H14; D05-H16A; D05-H17A6; D05-H17C

TECH UPTX: 20030121

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques.

Preferred Nucleic Acid: (II) preferably comprises the nucleotide sequence of (S3) or (S4), encodes an amino acid sequence of (S1) or (S2), or comprises a sequence complementary to the above mentioned sequences. (II) further comprises vector nucleic acid sequences, and also comprises a nucleic acid sequence encoding a heterologous **polypeptide**.

Preferred Host Cell: (III) is a mammalian or non-human mammalian host cell.

Preferred **Polypeptide**: (I) comprises a sequence of (S1) or (S2) and further comprises heterologous amino acid sequences.

Preferred Method: In (M2), the presence of (II) is detected in a sample comprising mRNA molecules.

ABEX UPTX: 20030121

WIDER DISCLOSURE - The following are disclosed:

(1) making vectors and host **cells** comprising (II);

(2) any and all nucleotide variations and resulting amino acid polymorphisms or variations in **cell death**-related sequence that are the result of natural allelic variation and that do not alter the functional activity of programmed **cell death** -related **polypeptides**;

(3) nucleic acid molecules encoding programmed **cell death**-related **polypeptides** having a nucleotide sequence differing from that of programmed **cell death**-related sequence;

(4) nucleic acid sequences encoding programmed **cell death**-related **polypeptide** having a sequence that differs from (S3) or (S4) created by introducing substitutions, additions or deletions into (S3) or (S4);

(5) chimeric or fusion proteins comprising (I);

(6) non-human transgenic animal overexpressing (II) or in which the endogenous expression of programmed **cell death**-related polynucleotide is deleted; and

(7) recombinant expression vector comprising (II).

ADMINISTRATION - Pharmaceutical compositions comprising (I), (II), (IV) are administered by parenteral, e.g. intravenous, intradermal, subcutaneous, oral, e.g. inhalation, transdermal, transmucosal or rectal route. Dosage of (I) ranges from 0.001-30 (preferably, 5-6) mg/kg body weight. (IV) is administered in dosages ranging from 0.1-20 mg/kg body weight. Modulator compounds identified using (I) are administered in dosages ranging from 1 microg-500 mg/kg (preferably, 1-50 microg/kg).

EXAMPLE - Smart Chip (RTM) microarray chip with brain-biased and programmed **cell death**-enriched clones was constructed by arraying approximately 7300 consolidated expressed sequence tag (EST) from two cDNA libraries cloned from rat frontal cortex and differentiated PC12 **cells** deprived of nerve growth factor (NGF), and 289 genes that were known markers for the central nervous system and/or programmed **cell death**. The levels of expression of the genes was monitored at 1,3,6,12 and 24 hours after K+ withdrawal. Regulated genes were then sorted by time course expression pattern to identify cellular processes mobilized by cerebellar granule neuron programmed **cell death** at the RNA level. Included in the analysis were expression profiles of many known pro- and anti-apoptotic regulatory proteins, including transcription factors, Bcl-2 family members, caspases, cyclins, heat shock proteins (HSPs), inhibitors of apoptosis (IAPs), growth factors and receptors, other signal transduction molecules, p53, superoxide

dismutases (SODs), and other stress response genes. The time courses of expression of regulated genes induced by K+ withdrawal in the presence or absence of serum was compared to time courses of expression induced by glutamate toxicity. A restricted set of relevant genes regulated by multiple models of programmed **cell death** in cerebellar granule neurons was identified, and these genes included the rat NARC10 and the rat NARC16. NARC10 encoded an approximately 2 kilobase mRNA transcript having the corresponding cDNA which has a fully defined sequence of 2034 nucleotides (S3) as given in specification. This transcript had a 549 nucleotide open reading frame (nucleotides 95-643 of (S3)), which encodes a 182 amino protein. An analysis of the full-length NARC10 **polypeptide** using the PSORT protein localization algorithm predicted a nuclear localization. NARC16 encoded an approximately 3.2 kb mRNA transcript having the corresponding cDNA which has a fully defined sequence of 3206 nucleotides (S4) as given in specification. This transcript had a 2019 nucleotide open reading frame (nucleotides 145-2163 of (S4)), which encoded a 672 amino acid protein. A second, brain-restricted isoform of NARC16 that was 1 kilobase larger than the most abundant form was detected by Northern blotting.

L110 ANSWER 2 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2002-643398** [69] WPIX
DNC **C2002-181718**
TI Identifying regulator **polypeptides** which influence target transcriptional regulatory regions, useful for treating cancer, comprises introducing host cells expressing the **polypeptide** into a library of polynucleotides.
DC B04 D16
IN SMITH, E S; ZAUDERER, M
PA (UYRP) UNIV ROCHESTER
CYC 100
PI WO 2002062822 A2 20020815 (200269)* EN 224p C07K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002192675 A1 20021219 (200303) C12Q001-68
ADT WO 2002062822 A2 WO 2002-US2814 20020204; US 2002192675 A1 Provisional US 2001-265589P 20010202, Provisional US 2001-265880P 20010205, Provisional US 2001-271423P 20010227, US 2002-61395 20020204
PRAI US 2001-271423P 20010227; US 2001-265589P 20010202; US 2001-265880P 20010205; US 2002-61395 20020204
IC ICM C07K000-00; C12Q001-68
ICS C12N015-87; G01N033-53; G01N033-567
AB WO 200262822 A UPAB: 20021026
NOVELTY - Identifying polynucleotides encoding a regulator **polypeptide**, whose expression induces activation of a target transcriptional regulatory region in a host **cell**, comprising providing a population of eukaryotic host **cells** capable of expressing the **polypeptide**, introducing into the host **cell** a library of polynucleotides encoding the **polypeptides**, permitting expression of the **polypeptides**, and recovering them from the host **cells**, is new.

DETAILED DESCRIPTION - Identifying polynucleotides encoding a regulator **polypeptide**, whose expression induces activation of a target transcriptional regulatory region in a host **cell**, comprising:

(a) providing a population of eukaryotic host **cells** capable of expressing the regulator **polypeptide**, where the host **cells** comprise a target transcriptional regulatory region which is

naturally induced in a target cellular process, where the target transcriptional regulatory region is operably associated with a polynucleotide encoding a gene product, the expression of which results in host **cell death** or cause the host **cells** to exhibit pre-determined modified phenotype, and where the gene product is expressed upon activation of target transcriptional regulatory region;

(b) introducing into the population of host **cells** a library of polynucleotides constructed in a poxvirus vector, encoding, through operable association with a vector or the poxvirus transcriptional regulatory region, candidate regulator **polypeptides**, each candidate regulator **polypeptide** comprising:

(i) a candidate **peptide**; and

(ii) a molecular scaffold fused to the **peptide** so that the **peptide** is displayed on the surface of the candidate regulator **polypeptide**;

(c) permitting expression of the plurality of candidate regulator **polypeptides** in the host **cells** under conditions where host **cell death** or the modified phenotype can be detected; and

(d) recovering polynucleotides of the library from those individual host **cells** which undergo **cell death**, or the poxvirus vector particles comprising the polynucleotides from the host **cells** which exhibit or failed to exhibit the modified phenotype.

INDEPENDENT CLAIMS are also included for the following:

(1) a kit for the identification of the regulator **polypeptide**, comprising a library of the novel polynucleotides and a population of eukaryotic host **cells**, where the polynucleotides encoding the **polypeptides** are recoverable from individual host **cells** which undergo **cell death** or which exhibit or failed to exhibit the modified phenotype;

(2) an isolated polynucleotide which encodes a regulator **polypeptide**, produced by the novel method; and

(3) a composition comprising the regulator **polypeptide** and a carrier.

ACTIVITY - Cytostatic; Antiarrhythmic; Cardiant; Vasotropic; Anorectic; Neuroprotective; Osteopathic; Antipsoriatic; Antibacterial; Virucide; Anti-HIV (human immunodeficiency virus); Vulnerary.

No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The methods are useful in selecting and/or **screening** regulator molecules, such as **polypeptides**, which directly or indirectly induce or suppress the transcriptional activation of a target transcriptional regulatory region in a eukaryotic host **cell**. These regulator molecules may be used in preventing or treating cancers (e.g. breast or ovarian cancer), cardiovascular diseases (e.g. arrhythmia, heart failure, ischemia), obesity, neurodegenerative diseases (e.g. Alzheimer's disease), bone pathologies, dermatologic diseases (e.g. psoriasis), infections (e.g viral, bacterial), acquired immunodeficiency syndrome (AIDS), in cosmetic applications, and in wound healing. The method is also useful in **screening** regulator molecules that block antibiotic transport mechanisms, in drug toxicities and drug resistance applications, and in improving the performance of existing or developmental drugs. It may also be used in immunobiology, inflammation, allergic response, and in biotechnology applications.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-E03B; B04-E08; B04-F0100E; B04-F1100E; B04-N0200E; B11-C08E5; **B12-K04E**; B14-A01; B14-A02; B14-A02B1; B14-E12; B14-F01A; B14-F01B; B14-F02D; B14-G01B; B14-H01; B14-H01B; B14-J01A4; B14-N01; B14-N17B; B14-N17C; B14-S03A; **D05-H08**; **D05-H09**; D05-H12A; D05-H12E; D05-H14; D05-H17

TECH UPTX: 20021026

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Identifying polynucleotides encoding a regulator **polypeptide** further comprises:
(a) providing a population of eukaryotic host **cells** capable of expressing the regulator **polypeptide**, where the host **cells** comprise a target transcriptional regulatory region which is naturally induced in a target cellular process, where the target transcriptional regulatory region is operably associated with a polynucleotide encoding a selectable gene product, the expression of which results in host **cell death**, and where selectable gene product is expressed upon activation of the target transcriptional regulatory region;
(b) introducing the recovered polynucleotides into the population of host **cells**;
(c) permitting expression of candidate regulator **polypeptides** encoded by recovered polynucleotides in the population of host **cells** under conditions where host **cell death** can be detected; and
(d) recovering polynucleotides of the library from those individual host **cells** which undergo **cell death**.
This method also comprises repeating steps (a)-(d) one or more times, thus, enriching for polynucleotides of the library. It may also comprise isolating those recovered polynucleotides. The expression of the selectable gene product results in **cell death** through a process of irreversible growth inhibition, apoptosis, or **cell** lysis. The candidate **peptide** comprises a random chain of at least 4 amino acids. The molecular scaffold comprises a conformation or motif, such as a beta-sandwich motif, a zinc finger motif, or an alpha-helical bundle motif. This scaffold is an immunoglobulin **polypeptide** or its fragment. It is selected from a minibody, tendamistat, a CP1 zinc finger, a staphylococcal protein A analog Z domain, a pancreatic secretory trypsin inhibitor (PSTI), a synthetic coiled coil, a human lipoprotein-associated coagulation inhibitor (LACI-DI), and a cytochrome b562 protein, and preferably, fibronectin type III domain (FN3). The candidate **peptide** is fused into a region consisting of the FN3 BC loop, the FN3 FG loop, the FN3 terminal tail, and a combination of two or more of these regions. The combination comprises the FN3 BC loop and the FN3 FG loop. The candidate regulator **polypeptides** further comprise one or more fusion partners. The target cellular process comprises cellular differentiation, growth regulation, apoptosis, or hormonal response. The expression of the selectable gene product directly or indirectly induces apoptosis. The gene product comprises a **death** domain containing receptor expressed on the surface of the host **cells**, and where the host **cells** are contacted with a ligand specific for the **death** domain containing receptor. The expression of this gene product may also result in a cytotoxic T-lymphocyte induced lytic event. The target transcriptional regulatory region is operably associated with a polynucleotide encoding a target epitope for a cytotoxic T lymphocyte (CTL). The target epitope is expressed on the surface of the host **cells** in the context of a native Major Histocompatibility Complex (MHC) molecule expressed on the host **cell**, and where the host **cells** are contacted with CTLs which are restricted for the MHC molecule and specific for the target epitope. The expression of the selectable gene product also results in **cell** suicide. The target transcriptional regulatory region is operably associated with a polynucleotide encoding the heterologous suicide protein. This heterologous suicide protein comprises a protein such as a diphtheria **toxin** A chain **polypeptide**, a Pseudomonas **exotoxin** A chain **polypeptide**, a ricin A chain **polypeptide**, an abrin A chain **polypeptide**, a modeccin A chain **polypeptide**, or an alpha-sarcin **polypeptide**. The library of polynucleotides is introduced into the population of eukaryotic

host **cells** by means of a eukaryotic virus vector. The population of eukaryotic host **cells** are infected with the library at a multiplicity of infection ranging from 1-10. The eukaryotic virus vector is an animal virus vector or a plant virus vector which is capable of producing infectious virus particles in mammalian **cells**. The naturally-occurring genome of the vector is a linear, double-stranded DNA. The vector is an adenovirus vector, a herpesvirus vector or preferably, a poxvirus vector. The poxvirus vector is preferably an orthopoxvirus vector, or may also be an avipoxvirus vector, a capripoxvirus vector, a leporipoxvirus vector, an entomopoxvirus vector, or a suipoxvirus vector. The orthopoxvirus vector consists of a raccoon poxvirus vector, and preferably a vaccinia virus vector. The host **cells** are permissive for the production of infectious virus particles of the attenuated vaccinia virus vector. The vaccinia virus vector is deficient in D4R synthesis. The vector transcriptional regulatory region of the library of polynucleotides functions in the cytoplasm of a poxvirus-infected **cell**. This transcriptional regulatory region comprises a constitutive promoter, specifically, a vaccinia virus p7.5 promoter. The promoter is a synthetic early/late promoter. It is a T7 phage promoter active in **cells** in which T7 RNA polymerase is expressed. The vector transcriptional regulatory region also comprises a transcriptional termination region. The library of polynucleotides is constructed by:

(a) providing a population of host **cells** permissive for the production of infectious viral particles of the eukaryotic virus vector;

(b) cleaving an isolated linear DNA fragment comprising the genome of the eukaryotic virus vector to produce a first viral fragment and a second viral fragment, where the first fragment is nonhomologous with the second fragment;

(c) providing a population of transfer plasmids comprising polynucleotides encoding the plurality of candidate regulator **polypeptides** through operable association with a transcription control region, where each of the polynucleotides is flanked by a 5' flanking region and a 3' flanking region, where the 5' flanking region is homologous to the first viral fragment and the 3' flanking region is homologous to the second viral fragment;

(d) introducing the transfer plasmids and the first and second viral fragments into the population of host **cells** under conditions where each of the transfer plasmids, first viral fragment, and second viral fragment undergo in vivo homologous recombination, thus, producing a population of **viable** modified virus genomes, each comprising a polynucleotide which encodes a candidate regulator **polypeptide**; and

(e) recovering the population of modified virus genomes.

Additionally, identifying polynucleotides encoding a regulator **polypeptide** further comprises:

(a) providing a population of eukaryotic host **cells** capable of expressing the regulator **polypeptide**, where the host **cells** comprise a target transcriptional regulatory region which is naturally induced in a target cellular process, where the target transcriptional regulatory region is operably associated with a polynucleotide encoding a selectable gene product, the expression of which causes the host **cells** to exhibit a predetermined modified phenotype, and where the gene product is expressed upon activation of the target transcriptional regulatory region;

(b) introducing the recovered poxvirus vector particles into the population of host **cells**;

(c) permitting expression of candidate regulator **polypeptides** encoded by the recovered polynucleotides in the host **cells** under conditions where modified phenotype can be detected; and

(d) recovering poxvirus particles comprising polynucleotides of the library from those individual host **cells** selected from the group consisting of host **cells** which exhibit the modified phenotype,

and those host **cells** which fail to exhibit the modified phenotype.
The steps may be repeated one or more times, thus, enriching for polynucleotides of the library. It further comprises isolating polynucleotides of the library from the recovered poxvirus vector particles. The expression of the regulator **polypeptide** influences the activation of the target transcriptional regulatory region by inducing activation, and where poxvirus particles are recovered from those host **cells** which exhibit the modified phenotype. In addition, the expression of the regulator **polypeptide** influences the activation of the target transcriptional regulatory region by suppressing the activation, and where poxvirus particles are recovered from those host **cells** which fail to exhibit the modified phenotype.

L110 ANSWER 3 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2002-479717** [51] WPIX
DNC **C2002-136538**
TI Novel programmed **cell death** modulating proteins, useful for treating or preventing disorders associated with abnormal **cell proliferation** and apoptosis such as cancer, stroke, Parkinson's disease, myocardial infarction.
DC B04 D16
IN BAEHRECKE, E H
PA (UYMA-N) UNIV MARYLAND BIOTECHNOLOGY INST; (BAEH-I) BAEHRECKE E H
CYC 96
PI WO 2002034882 A2 20020502 (200251)* EN 88p C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2002027378 A 20020506 (200257) C12N000-00
US 2002142443 A1 20021003 (200267) C12N009-64
ADT WO 2002034882 A2 WO 2001-US48053 20011029; AU 2002027378 A AU 2002-27378 20011029; US 2002142443 A1 Provisional US 2000-243865P 20001027, US 2001-16768 20011029
FDT AU 2002027378 A Based on WO 200234882
PRAI US 2000-243865P 20001027; US 2001-16768 20011029
IC ICM C12N000-00; C12N009-64
ICS A61K038-48
AB WO 200234882 A UPAB: 20020812
NOVELTY - A **polypeptide** (I) that modulates programmed **cell death**, comprising a 53, 53, 54, 53, 53 (S1-S5), or 442 (S8) residue amino acid sequence, given in specification, is new. (S1) is 53 amino acid domain in Drosophila E93, that is conserved in human (S2), the fish T. nigroviridis (S3), the mouse Mus musculus (S4) and the nematode Caenorhabditis elegans (S5).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a composition (II) comprising (I) and carrier;
(2) an apoptotically active **polypeptide** (III) having at least 60 % amino acid identity over the complete amino acid sequence of (S1);
(3) treating or preventing (M1) a disorder associated with a decrease in apoptosis, involves administering a pharmaceutical composition comprising an apoptotically active protein having an amino acid sequence of (S1) or with at least 60 % homology to (S1);
(4) a polynucleotide (IV) that encodes for a protein that modulates apoptosis, where the polynucleotide comprises a 4958, 6704, or 9574 nucleotide sequence, given in the specification;
(5) an apoptotically active polynucleotide that hybridizes at least

one nucleotide sequence of (IV) under high stringency conditions;

(6) an apoptotically active polynucleotide that has at least 90% homology (IV);

(7) detecting a polynucleotide encoding a protein having an amino acid sequence of (S1)-(S5) or (S8) in a biological test sample containing nucleic acids, comprising:

(a) mixing at least a fragment of a complement of the polynucleotide sequence encoding at least a fragment of a protein having at least one amino acid sequence of (S1)-(S5) or (S8) with the biological test sample containing nucleic acids, to form a resulting mixture;

(b) subjecting the mixture to conditions such that hybridization will occur between the biological test sample and the complement of the polynucleotide sequence encoding at least a fragment of a protein having at least one amino acid sequence of (S1)-(S5) or (S8); and

(c) detecting hybridization complexes in the mixture subjected to hybridization conditions, where the presence of a hybridization complex correlates with the presence of a polynucleotide encoding a protein having at least one amino acid sequence of (S1)-(S5) or (S8) in the biological test sample;

(8) an expression vector (V) containing at least a fragment of a polynucleotide sequence which encodes an amino acid sequence of (S1)-(S5) or (S8) or its complement;

(9) a transformed host **cell** (VI) containing (V);

(10) a purified antibody (VII) which binds to (I); and

(11) a vaccine comprising a polynucleotide sequence that encodes (I).

ACTIVITY - Cytostatic; Anti-HIV (human immunodeficiency virus); Nootropic; Neuroprotective; Immunostimulant; Antianemic; Vasotropic; Cardiant; Cerebroprotective.

MECHANISM OF ACTION - Apoptosis modulator; Gene therapy; Vaccine.

The open reading region of the hE93 gene was placed into a tissue culture **cell** transfection vector so that hE93 would be expressed in **cells** to test if expression of the hE93 expressed protein is sufficient to induce programmed **cell death**. As controls, **cells** were transfected with an empty vector, the same vector except that it contains either green fluorescent protein (GFP) which was used to monitor transfection rate, the proapoptotic protein Bax which was sufficient to induce programmed **cell death**, or the antiapoptotic protein Bcl-xl Adams and Cory, 1998). Each of these gene constructs were transfected into equal numbers of Bovine BHK, human MCF7, and human 293T **cell** lines. Nineteen hours post transfection the **cell viability** was assayed. The empty vector and GFP constructs did not significantly impact **cell viability**. In contrast, expression of Bax significantly reduced the **viability** of all 3 **cell** lines as has been previously demonstrated for this proapoptotic protein. The antiapoptotic protein Bcl-xl had some impact on the **viability** of BHK and 293T **cells**. hE93 protein expression was the most potent inducer of **cell death** in the human MCF-7 and 293T **cell** lines, but did not induce significant levels of **cell death** in the bovine **cells**. The data indicate that expression of the hE93 gene is sufficient to induce apoptosis.

USE - (I) is useful for **screening** a potential cellular apoptosis inhibiting compound for determining its use as therapeutic agent for treatment of diseases associated with increased programmed **cell death** which involves contacting a **cell** which expresses a protein including an amino acid sequence of (S1)-(S5) or (S8) with a test compound and determining the level of apoptosis activity of the **cell**, where a decrease in activity identifies a compound that inhibits apoptotic activities. A (II) having (I) which has a sequence of (S1)-(S5) or (S8) is useful for treating or preventing a disorder associated with a decrease in apoptosis. (All claimed). (I) is useful for treating or preventing cancer e.g. adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, etc. Inhibition of (I) activity is useful for treating

disorders associated with increase in **cell death** or apoptosis, thus stimulating **cell proliferation**. Thus inhibition of (I) activity is useful for treating acquired immunodeficiency syndrome (AIDS) and other infectious or genetic immunodeficiencies, neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amytotropic lateral sclerosis, retinitis pigmentosa, and cerebellar degeneration, myelodysplastic syndromes, such as aplastic anemia, ischemic injuries, such as myocardial infarction, stroke, and reperfusion injury, **toxin**-induced diseases, etc. (IV) is useful in ex vivo gene therapy techniques, and polynucleotide sequences encoding **polypeptide** sequences of (S1)-(S5) or (S8) may be employed as hybridization probes or as primers.
Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-C01G; B04-E01; B04-E03F; B04-E05; B04-E08; B04-F0100E; B04-G01; B04-N02A0E; B11-C07B; B11-C08E5; **B12-K04E**; **B12-K04F**; B14-A02B1; B14-F01B; B14-F02D; B14-F02D1; B14-F03; B14-F05; B14-H01; B14-H01A; B14-H01B; B14-J01A3; B14-J01A4; B14-N03; B14-N16; B14-S03A; B14-S11; D05-C12; D05-H07; **D05-H09**; D05-H11; D05-H12A; D05-H12D1; D05-H12E; D05-H14; D05-H17A6

TECH UPTX: 20020812

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques.
Preferred Composition: (II) comprises (I) which has a sequence of (S2) or (S8).
Preferred **Polypeptide**: (III) has a sequence of (S2-S5), or (S8).
Preferred Method: In (M1), the pharmaceutical composition comprises apoptotically active protein having a sequence of (S1) or with at least 60 % homology to (S1), where the homologous sequence comprises a sequence of (S2-S5) or (S8). Preferably, the homologous amino acid sequence is (S2).
Preferred Host Cell: (VI) has been cultured for expression of the **polypeptide** in recoverable form.

ABEX UPTX: 20020812

WIDER DISCLOSURE - A variant of **polypeptides** having sequence of (S1)-(S5) or (S8), where the variant exhibits at least 80, preferably 90 % identity with the **polypeptide** sequences, is also disclosed.

ADMINISTRATION - (I) is administered by intravenous, intramuscular, intraarterial injection, or infusion techniques. No dosage is given.
EXAMPLE - A proposed Drosophila E93 gene which has a 9567 nucleotide sequence (S12), given in specification, was first identified based on its induction by the steroid 20-hydroxyecdysone (ecdysone) just prior to programmed **cell death** of larval salivary glands. At the time the first proposed E93 gene was isolated, no similar genes had been identified. However, subsequent to the isolation of the first proposed E93 gene an error was discovered in the original gene sequence that had a marked effect on the predicted E93 protein which has a 1221 residue amino acid sequence (S11), given in specification. Specifically, the omission of a nucleotide that changed the reading frame encoded for an amino acid sequence markedly different from that of the method. The amino acid residue in sequence (S11) ranging from 776 to and including 956 had since been determined to be incorrect. The recently identified and corrected gene sequence which has a 9574 nucleotide sequence, given in specification, was used to identify 53 amino acid domain in Drosophila E93 sequence, given in specification that was conserved in the human Homo sapiens, the fish T. nigroviridis, the mouse Mus musculus and the nematode Caenorhabditis elegans. Animals that possess mutation in E93 had defects in programmed **cell death**, and their salivary glands do not die. E93 protein binds to chromosomes, and E93 mutants exhibit defects in **cell death** gene transcription including the caspase dronc. Furthermore, expression of E93 was sufficient to induce programmed **cell death** in difference Drosophila **cells**

types during development. Previously isolated steroid-regulated genes that function in programmed **cell death** also regulate **cell** differentiation and morphogenesis in Drosophila while E93 appears to function more specially in **cell** killing. Combined, these data indicated that Drosophila E93 regulates programmed **cell death** by regulating the transcription of programmed **cell death** genes. The human E93 (hE93) gene had been characterized and found to include two distinct RNAs based on the isolation of related but independent cDNAs. One cDNA was isolated from a human testis library and other cDNA from a fetal brain library. These cDNAs were sequenced on both strands and were identical in most of their sequence, but possessed different 5' ends. The cDNA isolated from testis encoded a 4958 base RNA (S6) that had been named hE93A, and the cDNA isolated from fetal brains encoded a 6074 base (S7) RNA that had been named hE93B. These sequences mapped to the same region of human chromosome 4, and were alternative transcript forms of hE93. The transcripts utilized alternative promoters and splicing, but encoded identical predicted proteins. In (S6), bases 1-690 encoded the hE93A-specific region and in (S7), the hE93B- specific region included bases 1-819. The remaining bases in both (S3) and (S7) encoded for the same **polypeptide** comprising a 53 amino acid domain that was conserved between Drosophila hE93 and the human hE93 protein. Specifically, bases 1547 to 1705 in (S6) and bases 2676 to 2384 in (S7) were conserved with the amino acid domain of Drosophila E93.

L110 ANSWER 4 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN 2002-041408 [05] WPIX
CR 2001-611741 [70]; 2002-049281 [06]
DNN N2002-030721 DNC C2002-011780
TI Novel protein kinase nucleic acid molecules and the encoded proteins for diagnosing and treating cellular proliferative, bone, immune, cardiovascular, liver, pain or metabolic disorders and identifying modulators.
DC B04 D16 S03
IN HUNTER, J J; MEYERS, R
PA (MILL-N) MILLENNIUM PHARM INC
CYC 96
PI WO 2001081589 A2 20011101 (200205)* EN 115p C12N015-54 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001057405 A 20011107 (200219) C12N015-54 <--
EP 1297151 A2 20030402 (200325) EN C12N015-54 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001081589 A2 WO 2001-US13785 20010425; AU 2001057405 A AU 2001-57405 20010425; EP 1297151 A2 EP 2001-930916 20010425, WO 2001-US13785 20010425
FDT AU 2001057405 A Based on WO 200181589; EP 1297151 A2 Based on WO 200181589
PRAI US 2000-593927 20000615; US 2000-199391P 20000425
IC ICM **C12N015-54**
ICS **C07K016-40; C12N005-10; C12N009-12;** C12Q001-68; G01N033-50
AB WO 200181589 A UPAB: 20030416
NOVELTY - An isolated protein kinase **polypeptide**, (I), termed as 14911, comprising a sequence (S1) of 397 amino acids, its naturally occurring allelic variant encoded by a nucleic acid molecule (NA) which hybridizes to a NA having a sequence (S2) of 1191 or 1281 bp given in specification or its complement, a **polypeptide** encoded by a NA having a sequence 60% identical to (S2) or a fragment of (I), is new.
DETAILED DESCRIPTION - (I) is chosen from a fragment of (S1) comprising 15 contiguous amino acids, naturally allelic variant of (S1)

encoded by a NA which hybridizes to (S2) or its complement, a **polypeptide** encoded by a NA 60% identical to (S2) or the nucleotide sequence of the DNA insert of the plasmid deposited with specific ATCC Accession Number or its complement. INDEPENDENT CLAIMS are included for the following:

(1) an isolated 14911 NA (II) comprising (S2) or a sequence 60% identical to (S2) or a nucleotide sequence of the DNA insert of the plasmid deposited with specific ATCC Accession Number, a NA comprising a fragment of 15 nucleotides of (S2) or a NA encoding (I);

(2) a host **cell** (III) which contains (II);

(3) an antibody (IV) that specifically binds to (I);

(4) producing (I);

(5) detecting the presence of (I) or (II) in a sample, by contacting the sample with a compound which selectively hybridizes to (II) or binds to (I) and determining whether the compound hybridizes to (II) or binds to (I) in the sample;

(6) a kit comprising a compound which selectively hybridizes to (II) or binds to (I) and instructions for use;

(7) modulating the activity of (I), by contacting (I) or **cell** expressing (I) with a compound which binds to the **polypeptide** to modulate the activity of (I);

(8) identifying a **polypeptide** associated with cancer or a cellular **proliferation** and/or differentiation disorder, by contacting a sample comprising **polypeptides** with a 14911 partner of (I) and detecting the presence of **polypeptide** in the sample that binds to the 14911 binding partner;

(9) identifying a subject having a cancer or a cellular **proliferation** and/or differentiation disorder, or at risk for developing cancer or a cellular **proliferation** and/or differentiation disorder, by contacting sample obtained from the subject comprising **polypeptides** with a 14911 modulator and detecting the presence of **polypeptide** in the sample that binds to the modulator; and

(10) treating (M1) a subject having cancer or a cellular **proliferation** and/or differentiation disorder or at risk of developing the disorder, by administering a 14911 modulator of (I) or (II).

ACTIVITY - Cytostatic; anorectic; immunosuppressive; antiarthritic; antirheumatic; antiasthmatic; antiallergic; analgesic; antipsoriatic; antidiabetic; antiatherosclerotic; ophthalmological; gynecological; antiarrhythmic; antianemic; antithyroid; hypotensive; osteopathic; immunomodulator; virucide; cardiant; antiinflammatory; hepatotropic.

MECHANISM OF ACTION - Gene therapy; Modulator of **cell proliferation**, differentiation, growth and division. No supporting data is given.

USE - (I) is useful for identifying a compound which binds to or modulates the activity of (I), by contacting (I) or **cell** expressing (I) with a test compound and determining whether the **polypeptide** binds to the test compound. Fragments comprising at least 25 contiguous nucleotides of (II) are useful as hybridization probes or primers for identifying a nucleic acid molecule associated with cancer or a cellular **proliferation** and/or differentiation disorder and a subject having a cancer or a cellular **proliferation** and/or differentiation disorder or at risk for developing the disorder. Assaying the ability of the compound to modulate 14911 nucleic acid expression or 14911 **polypeptide** activity is useful for identifying a compound capable of treating cancer or a cellular **proliferation** and/or differentiation disorder characterized by aberrant 14911 nucleic acid expression or **polypeptide** activity. Assessing the expression of (I) or (II) is useful for evaluating the efficacy of a treatment of a cancer or a cellular **proliferation** and/or differentiation disorder and diagnosing the disorder in a subject. (M1) is useful for treating lung, colon, brain and breast cancer (claimed). (I) and (II) are

useful as modulating agents in regulating cellular **proliferation**, growth, differentiation or division. (I) is involved in regulation of transmission of signals from cellular receptors, the modulation of entry of **cells** into mitosis, cellular differentiation, **cell death** and regulation of cytoskeleton function. (I) and (II) provide both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant or unwanted 14911 expression or activity e.g. a 14911-associated disorder which includes cellular **proliferation** /or differentiation disorders (e.g. cancer, carcinoma, leukemia or hematopoietic neoplastic disorder), disorders associated with bone metabolism (osteoporosis, osteomalacia, **rickets**), immune e.g. inflammatory (autoimmune diseases for e.g. diabetes mellitus, arthritis, multiple sclerosis, autoimmune thyroiditis, psoriasis, dermatitis, asthma, allergic asthma, aplastic anemia, Grave's disease, chronic active hepatitis), cardiovascular disorders (e.g. hypertension, atherosclerosis, arrhythmia, heart failure), including endothelial **cell** disorders (psoriasis, diabetic retinopathy, endometriosis, rheumatoid arthritis), liver disorders (hepatocellular necrosis and injury), viral diseases, pain and metabolic disorders (obesity, anorexia, cachexia, lipid disorders and diabetes). (I) is useful as an immunogen to generate antibodies which are useful to isolate, detect, purify 14911, for diagnostically monitoring protein levels for e.g. to determine the efficacy of a given treatment regimen and to modulate 14911 activity. 14911 protein is useful to **screen** for naturally occurring 14911 substrates. (II) is useful for expressing 14911 protein, to detect 14911 mRNA, or a genetic lesion in a 14911 gene and to modulate 14911 activity. 14911 NA sequences are also useful for identifying a **cell** or tissue type in a biological sample, chromosome mapping, in prognostic assays, to amplify DNA sequences from very small biological samples such as tissues e.g. hair or skin or body fluids in forensic biology and as primers and probes for use in identifying and/or cloning 14911 homologs in other **cell** types. 14911 molecules are also useful as pharmacogenomic markers. (III) is useful for producing non-human transgenic animals which are useful for studying the function and/or activity of 14911 and for identifying and/or evaluating modulators of 14911 activity. Compounds that modulate expression and/or activity of (I) are useful for treatment and diagnosis of kinase-related disorders.

Dwg.0/14

FS CPI EPI

FA AB; DCN

MC CPI: B04-E02E; B04-E03E; B04-E06; B04-E08; B04-F01QOE; B04-G03; B04-L04; B11-A01; B11-C08; B11-C08E5; **B12-K04A1**; **B12-K04E**; **B12-K04F**; B14-A02; B14-C01; B14-C03; B14-E11; B14-F01; B14-H01; B14-L06; B14-N01; B14-N03; B14-N07; B14-N10; B14-N11; B14-N12; B14-N17; B14-S03; D05-C03; D05-C07; **D05-H09**; D05-H11; D05-H12A; D05-H12B; D05-H12D2; D05-H12D4; D05-H12E; D05-H14; D05-H17A; D05-H17B; D05-H18

EPI: S03-E14H

TECH UPTX: 20020123

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by culturing (III) in an appropriate culture medium to produce the **polypeptide** (claimed). Preferred Method: In (M1), the modulator is a small molecule, **peptide**, **phosphopeptide**, anti-14911 antibody, a 14911 **polypeptide** comprising (S1) or its fragment, a 14911 **polypeptide** comprising an amino acid sequence which is 90% identical to (S1), where the percent identity is calculated using the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 or an isolated naturally occurring allelic variant of (S1), which is encoded by NA which hybridizes to a complement of NA consisting of (S2), at 6XSSC at 45degreesC followed by one or more washes in 0.2XSSC, 0.1% SDS at 65degreesC, ribozyme, an antisense 14911 NA, NA encoding

polypeptide which is 90% identical to (S1), a NA encoding naturally occurring allelic variant of (I) or a gene therapy vector.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can also be prepared by standard synthetic chemistry.

ABEX UPTX: 20020123

WIDER DISCLOSURE - Also disclosed are:
(A) an isolated NA which is antisense to (II);
(B) detecting the presence of 14911 activity in a biological sample, by contacting with an agent capable of detecting an indicator of 14911 activity;
(C) 14911 chimeric or fusion proteins;
(D) vector comprising (II); and
(E) novel agents identified by **screening** assays using (I).

SPECIFIC SEQUENCES - (II) comprises a sequence of 1281 bp defined in the specification (claimed).

ADMINISTRATION - Administered by parenteral, e.g. intravenous, intradermal, subcutaneous, oral, transdermal, transmucosal or rectal route. Dosage not specified.

EXAMPLE - No relevant example is given.

L110 ANSWER 5 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN 2002-034511 [04] WPIX
DNC C2002-009708
TI Novel human aminotransferase **polypeptides**, nucleic acid molecules encoding the **polypeptide** for diagnosing, treating **cell proliferative**, bone, immune, liver, pain or metabolic disorders and identifying modulators.
DC B04 D16
IN CURTIS, R A J
PA (MILL-N) MILLENNIUM PHARM INC; (CURT-I) CURTIS R A J
CYC 95
PI WO 2001083720 A2 20011108 (200204)* EN 131p C12N009-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001059239 A 20011112 (200222) C12N009-00 <--
US 2002107192 A1 20020808 (200254) A61K048-00
ADT WO 2001083720 A2 WO 2001-US13786 20010425; AU 2001059239 A AU 2001-59239 20010425; US 2002107192 A1 Provisional US 2000-199379P 20000425, US 2001-843497 20010425
FDT AU 2001059239 A Based on WO 200183720
PRAI US 2000-199379P 20000425; US 2001-843497 20010425
IC ICM A61K048-00; **C12N009-00**
ICS A61K038-17; C07H021-04; **C12N005-06**; **C12N009-10**; **C12P021-02**
AB WO 200183720 A UPAB: 20020117
NOVELTY - An isolated human aminotransferase **polypeptide** (I), termed as 23686, comprising a sequence (S1) of 513 amino acids, its naturally occurring allelic variant encoded by a nucleic acid molecule (NA) that hybridizes to a NA having a sequence of 2427 (S2) or 1542 (S3) nucleotides or its complement, a **polypeptide** encoded by a NA having a sequence 60% identical to S2, S3 or a fragment of (I), is new.

DETAILED DESCRIPTION - (I) is chosen from a fragment of S1 comprising 15 contiguous amino acids, naturally allelic variant of S1 encoded by a NA which hybridizes to S2, S3 or its complement, a **polypeptide** encoded by a NA 60% identical to S2 or S3 or the nucleotide sequence of

the DNA insert of the plasmid deposited with specific ATCC Accession Number or its complement. INDEPENDENT CLAIMS are also included for the following:

(1) an isolated amino transferase NA (II) comprising S2 or S3, or a sequence having 60% identity to S2 or S3 or a nucleotide sequence of the DNA insert of the plasmid deposited with specific ATCC Accession Number, a NA comprising a fragment of 15 nucleotides of S2 or S3, or a NA encoding (I);

(2) a host **cell** (III) which contains (II);

(3) an antibody (IV) that specifically binds to (I);

(4) producing (I);

(5) detecting the presence of (I) or (II) in a sample, by contacting the sample with a compound which selectively hybridizes to (II) or binds to (I) and determining whether the compound hybridizes to (II) or binds to (I) in the sample;

(6) a kit comprising a compound which selectively hybridizes to (II) or binds to (I) and instructions for use;

(7) modulating the activity of (I), by contacting (I) or **cell** expressing (I) with a compound which binds to the **polypeptide** to modulate the activity of (I);

(8) identifying a **polypeptide** associated with a disorder, by contacting a sample comprising **polypeptides** with a 23686 partner of (I) and detecting the presence of **polypeptide** in the sample that binds to the 23686 binding partner;

(9) identifying a subject having a disorder, or at risk for developing a disorder, by contacting a sample obtained from the subject comprising **polypeptides** with a 23686 binding partner of (I) and detecting the presence of **polypeptide** in the sample that binds to 23686 binding partner, which identifies a subject having the disorder or risk for developing the disorder; and

(10) treating (M1) a subject having a disorder or at risk of developing a disorder, by administering a 23686 modulator of (I) or (II).

ACTIVITY - Cytostatic; Anorectic; Immunosuppressive; Antiarthritic; Antirheumatic; Antiasthmatic; Antiallergic; Analgesic; Antipsoriatic; Antidiabetic; Antiatherosclerotic; Ophthalmological; Gynecological; Antiarrhythmic; Antianemic; Antithyroid; Hypotensive; Osteopathic; Immunomodulator; Virucide; Cardiant; Antiinflammatory; Hepatotropic; Neuroprotective; Dermatological.

MECHANISM OF ACTION - Gene therapy; Modulator of **cell proliferation**, differentiation, migration and apoptosis; Modulator of (I). No supporting data is given.

USE - (I) is useful for identifying a compound which binds to or modulates the activity of (I), by contacting (I) or **cell** expressing (I) with a test compound and determining whether the **polypeptide** binds to the test compound. Fragments comprising at least 25 contiguous nucleotides of (II) having the sequence S2 are useful as hybridization probes or primers for identifying a nucleic acid molecule associated with a disorder and a subject having the disorder or at risk for developing the disorder. Assaying the ability of the compound to modulate 23686 nucleic acid expression or 23686 **polypeptide** activity is useful for identifying a compound capable of treating disorder characterized by aberrant 23686 nucleic acid expression or **polypeptide** activity. Assessing the expression level of (I) or (II) is useful for evaluating the efficacy of a treatment of a disorder and diagnosing the disorder in a subject. (M1) is useful for treating a subject having a disorder or at risk of developing a disorder (claimed). (I) and (II) are useful as modulating agents or as targets for developing modulating agents to regulate cellular **proliferation**, differentiation, migration and apoptosis. 23686 molecules play a role in cellular growth mechanisms including signal transmission from **cell** receptors, **cell** transversal through the **cell** cycle, **cell** differentiation, **cell** migration and patterning and programmed **cell death**. (I) and (II) provide both

prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant or unwanted 23686 expression or activity e.g. a 23686-associated disorder which includes cellular **proliferation**/or differentiation disorders (e.g. cancer, carcinoma, leukemia or hematopoietic neoplastic disorder), disorders associated with bone metabolism (osteoporosis, osteomalacia, **rickets**), immune e.g. inflammatory (autoimmune diseases for e.g. diabetes mellitus, arthritis, multiple sclerosis, autoimmune thyroiditis, psoriasis, dermatitis, asthma, allergic asthma, aplastic anemia, Grave's disease, chronic active hepatitis), cardiovascular disorders (e.g. hypertension, atherosclerosis, arrhythmia, heart failure), including endothelial **cell** disorders (psoriasis, diabetic retinopathy, endometriosis, rheumatoid arthritis), liver disorders (hepatocellular necrosis and injury), viral diseases including hepatitis B and C, pain and metabolic disorders obesity, anorexia, cachexia, lipid disorders and diabetes). (II) is useful for expressing 23686 protein, to detect 23686 mRNA, or a genetic lesion in a 23686 gene and to modulate 23686 activity. 23686 NA sequences are also useful for identifying a **cell** or tissue type in a biological sample, chromosome mapping, in prognostic assays and as primers and probes for use in identifying and/or cloning 23686 homologs in other **cell** types. (III) is useful for producing non-human transgenic animals which are useful for studying the function and/or activity of 23686 and for identifying and/or evaluating modulators of 23686 activity. Compounds that modulate expression and/or activity of (I) are useful to prevent, treat and ameliorate a disease.

Dwg.0/7

FS CPI

FA AB; DCN

MC CPI: B04-C01G; B04-E03E; B04-E05; B04-E06; B04-E08; B04-F0100E; B04-G03; B04-L04; B11-C08E; B11-C08E5; **B12-K04A; B12-K04F;** B14-A02; B14-A02A5; B14-A02A7; B14-C01; B14-C03; B14-C06; B14-C09; B14-D06; B14-E11; B14-E12; B14-F01; B14-F01A; B14-F02; B14-F02B; B14-F03; B14-F04; B14-F07; B14-G02; B14-G02A; B14-G03; B14-H01; B14-J01; B14-J01A4; B14-K01A; B14-N03; B14-N07; B14-N11; B14-N17C; B14-S01; B14-S03; B14-S04; **D05-H09**; D05-H11; D05-H12A; D05-H12D1; D05-H12D2; D05-H12E; D05-H14; D05-H17A3

TECH UPTX: 20020117

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by culturing (III) under conditions in which the nucleic acid molecule is expressed (claimed). Preferred Method: In (M1), the modulator is a small molecule, **peptide**, **phosphopeptide**, anti-23686 antibody, a 23686 **polypeptide** comprising S1 or its fragment, a 23686 **polypeptide** comprising an amino acid sequence which is 90% identical to S1, where the percent identity is calculated using the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 or an isolated naturally occurring allelic variant of S1, which is encoded by NA which hybridizes to a complement of NA consisting of S2, at 6X SSC at 45degreesC followed by one or more washes in 0.2X SSC, 0.1% SDS at 65degreesC, ribozyme, an antisense 23686 NA, nucleotide sequence of S2 or its fragment, NA encoding a **polypeptide** which is 90% identical to S1, a NA encoding naturally occurring allelic variant of (I) or a gene therapy vector.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can also be prepared by standard synthetic chemistry.

ABEX UPTX: 20020117

WIDER DISCLOSURE - Also disclosed are:
(1) an isolated NA which is antisense to (II);
(2) detecting the presence of 23686 activity in a biological sample, by contacting with an agent capable of detecting an indicator of 23686 activity;

(3) non-human orthologs of (I);
(4) 23686 chimeric or fusion proteins;
(5) vector comprising (II); and (6) novel agents identified by **screening** assays using (I).

SPECIFIC SEQUENCES - (II) comprises a sequence of 2427 or 1542 bp defined in the specification (claimed).

ADMINISTRATION - Administered by parenteral, e.g. intravenous, intradermal, subcutaneous, oral, transdermal, transmucosal or rectal route. Dosage is 0.001-30 mg/kg, preferably 5-6 mg/kg.

EXAMPLE - Human aminotransferase **polypeptides**, 23686, was expressed as a recombinant glutathione-S-transferase (GST) fusion **polypeptide** in Escherichia coli and the fusion **polypeptide** was isolated and characterized. Specifically, 23686 was fused to GST and the fusion **polypeptide** was expressed in E.coli, e.g., strain PEB199. Expression of the GST-23686-1 fusion protein in PEB199 was induced with isopropyl-B-D-thiogalactopyranoside (IPTG). The recombinant fusion **polypeptide** was purified from crude bacterial lysates of the induced PEB199 strain by affinity chromatography or glutathione beads. Using polyacrylamide gel electrophoretic analysis of the **polypeptide** purified from the bacterial lysates, the molecular weight of the resultant fusion **polypeptide** was determined.

L110 ANSWER 6 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN 2002-025874 [03] WPIX
DNN N2002-020009 DNC C2002-007205
TI New protective sequences and their products, useful for diagnosing and treating diseases involving **cell death**, including neurological disorders e.g. stroke and for identifying modulators of expression of the protective sequences.
DC B04 D16 P31
IN BARNEY, S; KATZ, L C; LO, D C; PORTBURY, S D; PURANAM, K; THOMAS, M B
PA (COGE-N) COGENT NEUROSCIENCE INC
CYC 94
PI WO 2001076457 A2 20011018 (200203)* EN 283p A61B000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001051508 A 20011023 (200213) A61B000-00
ADT WO 2001076457 A2 WO 2001-US11663 20010409; AU 2001051508 A AU 2001-51508 20010409
FDT AU 2001051508 A Based on WO 200176457
PRAI US 2000-547735 20000411
IC ICM A61B000-00
AB WO 200176457 A UPAB: 20020114
NOVELTY - An isolated protective sequence **polypeptide** (I) comprising an amino acid sequence chosen from 227 sequences (S1) of defined amino acids as given in the specification, designated CNI00734, CNI00735, CNI00737, CNI00739, CNI00741 or CNI00743, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated protective sequence nucleic acid molecule (II) encoding (I) and comprising a one of 227 fully defined nucleotide sequences (S2) as given in the specification, designated CNI00734, CNI00735, CNI00737, CNI00739, CNI00741 or CNI00743;
(2) an isolated nucleic acid molecule comprising a complement of (II);
(3) a(n) (expression) vector (III) comprising (II), operatively

associated with a regulatory nucleic acid controlling the expression of (II) in a host **cell**;

(4) a host **cell** (IV) genetically engineered to contain (II);

(5) a transgenic, non-human animal which has been genetically engineered to contain a transgene comprising (II);

(6) an isolated **polypeptide** comprising a sequence encoded by (II);

(7) an isolated fusion **polypeptide** comprising a fusion **peptide** and (I);

(8) an antibody (V) which binds to (I);

(9) treating (VI), ameliorating or preventing a protective sequence-mediated condition, disorder or disease in an individual, by administering a compound which modulates the function, activity, expression and/or level of a protective sequence, its product and/or protective sequence regulatory product in **cell**(s), tissue, organ, organism or individual;

(10) modulating the function, activity, expression and/or level of a protective sequence in a **cell**, by administering to the **cell** a compound which modulates the function, activity, expression and/or level of a protective sequence in the **cell**;

(11) a primer (VII) comprising an isolated nucleic acid molecule which hybridizes under highly stringent conditions to (II);

(12) diagnosing (VIII) a protective sequence-mediated condition, disorder or disease;

(13) identifying (IX) a compound which modulates expression of a protective sequence;

(14) transferring (X) a protective sequence into a **cell** comprising contacting the **cell** with (II); and

(15) a diagnostic kit for detecting a protective sequence-mediated condition, disorder or disease in an individual comprising a reagent comprising (V) or (VII) in suitable packaging.

ACTIVITY - Cerebroprotective; Vasotropic; Cytostatic; Nootropic; Neuroprotective; Antiparkinsonian; Antithyroid; Cardiant; Antiinflammatory; Antidiabetic; Antianemic; Hypotensive; Antiatherosclerotic; Antiulcer; Nephrotropic; Hepatotropic; Antisickling; Gynecological; Dermatological; Antipsoriatic; Osteopathic; Vulnerary; Tranquilizer; Immunosuppressive; Antiallergic; Antibacterial; Virucide; Fungicide; Protozoacide.

MECHANISM OF ACTION - Gene therapy. No supporting data is given.

USE - (VI) is useful for treating, ameliorating or preventing a protective sequence-mediated condition, disorder or disease, such as a disorder or disease of the central nervous system, in particular an ischemia-related condition such as stroke in a mammal, especially human (claimed). Protective sequences, their products or antibodies are useful diagnostically, prophylactically, therapeutically or as targets for treatment and diagnosis of conditions, disorders or diseases involving **cell death**. The protective sequences and their products are useful for preventing or treating disorders of the central nervous system including neurological and psychiatric conditions, cerebral edema, infections such as meningitis, degenerative diseases such as Alzheimer's, Huntington's, Parkinson's, idiopathic Parkinson's and motor neuron disease, demyelinating diseases such as multiple sclerosis, nutritional, environmental and metabolic conditions, diseases or disorders, conditions of the peripheral nervous system including diabetic neuropathy or peripheral nerve tumors, disorders or diseases which cause **cell death** in organ systems including blood vessels, heart (heart failure, ischemic or atherosclerotic heart disease, myocardial infarction), blood **cells** (autoimmune hemolytic anemia), white blood **cells**, lymph nodes, spleen, respiratory system (heart failure, pulmonary hypertension, adult respiratory distress syndrome, obstructive lung disease, asthma), oral cavity, gastrointestinal tract (stenosis, peptic ulcer, Crohn's disease), liver (hereditary

hyperbilirubinemia, hepatic circulation thrombosis, biliary cirrhosis) and biliary tract, pancreas (chronic pancreatitis), kidney (polycystic renal disease, acute glomerulonephritis, Goodpasture's syndrome, sickle **cell** disease, urolithiasis, nephropathy), lower urinary tract, upper urinary tract and bladder, male sexual organs and genitalia (congenital anomalies, balanoposthitis), female sexual organs and genitalia (endometriosis), breast (congenital anomalies, chronic mastitis, granuloma), thyroid gland (Hashimoto's thyroiditis), adrenal gland, parathyroid gland, skin (eczematous dermatitis, urticaria, graft-versus-host disease, psoriasis), musculoskeletal system (muscular atrophy, myositis, myasthenia gravis), bone marrow or bone (osteoporosis). Further the molecules are useful for treating conditions, diseases or disorders causing a fluid or hemodynamic rearrangement including systemic edema, edema from reduced oncotic pressure, cancer, inflammatory injury, inflammation, shock, burns, trauma and allergic reaction and inherited conditions, disorders and diseases including Down's syndrome, Klinefelter's syndrome, Turner's syndrome and inherited sex-linked conditions. The compositions are also useful for prevention or delay of **cell death** in one or more infections caused by bacteria, virus, members of the family **rickettsiae** or Chlamydia, fungi, yeast, hyphae, pseudohyphae, prions, protozoans or metazoans. The compositions promote **cell death** and are useful for treating and/or ameliorating cancer and autoimmune diseases.

Dwg.0/13

FS CPI GMPI

FA AB; DCN

MC CPI: B04-E03F; B04-E05; B04-E06; B04-E07; B04-E08; B04-F0200E; B04-G01; B04-N04A0E; B04-N08; B04-P0100E; B11-C07A; B11-C08E5; **B12-K04A; B12-K04F**; B14-A01; B14-A02; B14-A03; B14-A04; B14-C03; B14-E08; B14-E10C; B14-F01; B14-F02B; B14-F02D1; B14-F03; B14-F07; B14-G02D; B14-H01; B14-J01A3; B14-J01A4; B14-K01A; B14-N01; B14-N06; B14-N10; B14-N11; B14-N12; B14-N14; B14-N17A; B14-N17C; B14-S01; **D05-H09**; D05-H12A; D05-H12D1; D05-H12D2; D05-H12D4; D05-H12E; D05-H14B2; D05-H16A; D05-H17A6

TECH UPTX: 20020114

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by recombinant DNA technology.

Preferred Nucleic Acid: (II) encodes a protective sequence product. An isolated nucleic acid which hybridizes to (II) under moderate or highly stringent conditions is also preferred.

Preferred Vector: (III) is a viral vector.

Preferred **Cell**: (IV) is a neuronal **cell**, such as PC-12 **cell** or primary dissociated neuron. The transgene is expressed in the transgenic non-human animal.

Preferred Method: In (VI), the compound is a small organic molecule, an antibody, a ribozyme, an antisense molecule or their combinations. (VIII) comprises obtaining a biological sample from the individual, contacting the sample with (V), where if (V) interacts with the sample but does not interact with a sample from a control individual not undergoing a protective sequence-mediated condition, disorder or disease, indicates a positive diagnosis. Alternatively it comprises contacting the sample with (VII), where if (V) interacts with the sample but does not interact with a sample from a control individual not undergoing a protective sequence-mediated condition, disorder or disease, indicates a positive diagnosis. (IX) comprises contacting a test compound to a **cell** that expresses a protective sequence, measuring a level of protective sequence expression in the **cell** and comparing the level of protective sequence expression in the **cell** in the presence of the test compound to a level in the absence of the test compound, where if the level differs, a compound that modulates expression of a protective sequence is identified. In (X) the protective sequence is expressed in the **cell** and delays and/or prevents the **cell** from undergoing **cell death**.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can also be prepared by standard synthetic chemistry.

ABEX UPTX: 20020114

WIDER DISCLOSURE - Also disclosed are:
(1) allelic variants, homologs, mutants or fragments of (II);
(2) nucleic acid which encodes fusion proteins comprising protective sequence products or one or more protective sequence product domains fused to heterologous **polypeptide**;
(3) mimics, agonists and antagonists of the protective sequences, its products, genes, gene products or their regulatory elements; and
(4) antisense and ribozyme molecules directed against the protective sequences and their products.

ADMINISTRATION - Administered by inhalation, oral, buccal, parenteral or topical route. Dosage of (V) is 0.001-30 mg/kg, preferably 5-6 mg/kg.

EXAMPLE - A human fetal brain cDNA library in which individual clones were inserted into the NotI-SalI site of the pCMVSPORT2 vector was diluted 200000 fold in LB broth containing 0.2 mg/ml ampicillin. The diluted library was then plated and grown on LB agar. Single colonies were then used to inoculate deep-well blocks containing 1.5 ml LB broth containing 0.2 mg/ml ampicillin. Inoculated cultures were incubated at 37 degrees C with agitation at 150-200 repetitions per minute (rpm) for 18-24 hours. **Replicate** plates were created from the cultures. Remaining bacterial **cells** were centrifuged at 1000xg for 6 minutes to collect the **cells**. Plasmid DNA was extracted. Individual clones were chosen for their ability to delay or prevent **cell death** when introduced into a **cell** predisposed to undergoing **cell death**, relative to a corresponding **cell** into which no exogenous protective sequence had been introduced. The cDNA inserts of the clonally pure plasmids which were selected for their ability to protect **cells** from **cell death** when introduced into **cells** predisposed to undergo **cell death** were sequenced. The sequence data for the protective cDNA clones was compared using the basic local alignment search tool (BLAST) 2.0 algorithm. The BLAST nucleotide searches were performed with the BLASTN program to obtain homologous nucleic acids. BLAST protein searches of potential open reading frames (ORFs) was performed with the BLASTP program to obtain amino acid sequences homologous to the ORFs of the nucleic acid molecules. The results showed that 10 protective sequences were chosen based on their ability to prevent, delay, or rescue **cells** predisposed to undergo **cell death**, relative to a corresponding **cell** into which no exogenous protective sequence had been introduced. Protective sequence CNI00734, CNI00735, CNI00737, CNI00739, CNI00741, CNI00743, CNI00744, CNI00746, CNI00747 and CNI00749 comprised 927, 807, 225, 2135, 1105, 1434, 1752, 3064, 1350 and 1895 bp, respectively defined in the specification. 12, 8, 3, 34, 19, 29, 22, 40, 24 and 36 potential ORFs were identified within the protective sequences CNI00734, CNI00735, CNI00737, CNI00739, CNI00741, CNI00743, CNI00744, CNI00746, CNI00747 and CNI00749, respectively.

L110 ANSWER 7 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2001-032160** [70] WPIX
CR 1995-382985 [49]; 1997-503105 [46]; 1998-286866 [25]; 1999-229499 [19]; 1999-229532 [19]; 1999-229533 [19]; 1999-254381 [21]; 1999-254713 [21]; 1999-302739 [25]; 1999-326705 [27]; 1999-337420 [28]; 1999-347718 [29]; 1999-371118 [31]; 1999-404743 [34]; 1999-430385 [36]; 1999-551358 [46]; 1999-580306 [49]; 1999-620728 [53]; 2000-038358 [03]; 2000-062031 [05]; 2000-072883 [06]; 2000-116314 [10]; 2000-237871 [20]; 2000-271386 [23]; 2000-271431 [23]; 2000-271434 [23]; 2000-271435 [23]; 2000-292842 [25]; 2000-317943 [27]; 2000-412154 [35]; 2000-412324 [35]; 2000-412325 [35]; 2000-431586 [37]; 2000-442668 [38]; 2000-452188 [39]; 2000-452395 [39];

2000-499263 [44]; 2000-572269 [53]; 2000-572270 [53]; 2000-572271 [53]; 2000-587437 [55]; 2000-594320 [56]; 2000-594321 [56]; 2000-611443 [58]; 2000-611444 [58]; 2000-628263 [60]; 2000-638138 [61]; 2000-638201 [61]; 2000-679484 [66]; 2001-016509 [02]; 2001-025022 [03]; 2001-025251 [03]; 2001-025253 [03]; 2001-050025 [06]; 2001-050091 [06]; 2001-070561 [08]; 2001-071075 [08]; 2001-071078 [08]; 2001-071395 [08]; 2001-081051 [09]; 2001-090793 [10]; 2001-091968 [10]; 2001-103149 [11]; 2001-183260 [18]; 2001-226690 [23]; 2001-226823 [23]; 2001-235264 [24]; 2001-381383 [40]; 2001-381384 [40]; 2001-408281 [43]; 2001-451708 [48]; 2001-541567 [60]; 2001-541628 [60]; 2001-602746 [68]; 2001-625876 [72]; 2002-075461 [10]; 2002-090516 [12]; 2002-130120 [17]; 2002-130151 [17]; 2002-130882 [17]; 2002-171999 [22]; 2002-172001 [22]; 2002-205567 [26]; 2002-256031 [30]; 2002-280917 [32]; 2002-280928 [32]; 2002-280940 [32]; 2002-292065 [33]; 2002-362426 [39]; 2002-383270 [41]; 2002-404358 [43]; 2002-487624 [52]; 2002-657277 [70]; 2002-665999 [71]; 2002-673823 [72]; 2002-690475 [74]; 2002-713224 [77]; 2002-731348 [79]; 2002-740172 [80]; 2002-750461 [81]; 2003-066810 [06]; 2003-066893 [06]; 2003-066898 [06]; 2003-090845 [08]; 2003-102117 [09]; 2003-147434 [14]; 2003-147446 [14]; 2003-148238 [14]; 2003-155950 [15]; 2003-167072 [16]; 2003-174088 [17]; 2003-174140 [17]; 2003-174141 [17]; 2003-183819 [18]; 2003-183820 [18]; 2003-183821 [18]; 2003-183822 [18]; 2003-198285 [19]; 2003-201194 [19]; 2003-247083 [24]; 2003-275322 [27]; 2003-288106 [28]; 2003-288123 [28]; 2003-288142 [28]; 2003-288163 [28]

DNN **N2002-509255** DNC **C2002-181964**

TI PRO polynucleotides used to produce **polypeptides** used to target bioactive molecules such as **toxins**, radiolabels or antibodies, to specific **cells**, to cause targeted **cell death**.

DC B04 D16 S03

IN ASHKENAZI, A J; BAKER, K P; BOTSTEIN, D; DESNOYERS, L; EATON, D L; FERRARA, N; GERBER, H; GERRITSEN, M E; GODDARD, A; GODOWSKI, P; GRIMALDI, C J; GURNEY, A L; KLJAVIN, I J; NAPIER, M A; PAN, J; PAONI, N F; ROY, M A; STEWART, T A; TUMAS, D; WATANABE, C K; WILLIAMS, P M; WOOD, W I; ZHANG, Z; FONG, S; GODOWSKI, P J; GRIMALDI, J C

PA (GETH) GENENTECH INC

CYC 93

PI WO 2000073454 A1 20001207 (200104)* EN 933p C12N015-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000037743 A 20001218 (200118) C12N015-12
EP 1210418 A1 20020605 (200238) EN C12N015-12
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002137075 A1 20020926 (200270) C12Q001-68

ADT WO 2000073454 A1 WO 2000-US8439 20000330; AU 2000037743 A AU 2000-37743 20000330; EP 1210418 A1 EP 2000-916675 20000330, WO 2000-US8439 20000330; US 2002137075 A1 Provisional US 1997-49787P 19970616, Provisional US 1997-62250P 19971017, Provisional US 1997-65186P 19971112, Provisional US 1997-65311P 19971113, Provisional US 1997-66770P 19971124, Provisional US 1998-75945P 19980225, Provisional US 1998-78910P 19980320, Provisional US 1998-83322P 19980428, Provisional US 1998-84600P 19980507, Provisional US 1998-87106P 19980528, Provisional US 1998-87607P 19980602, Provisional US 1998-87609P 19980602, Provisional US 1998-87759P 19980602, Provisional US 1998-87827P 19980603, Provisional US 1998-88021P 19980604, Provisional US 1998-88025P 19980604, Provisional US 1998-88026P 19980604, Provisional US 1998-88028P 19980604, Provisional US 1998-88029P 19980604, Provisional US 1998-88030P 19980604, Provisional US 1998-88033P 19980604, Provisional US 1998-88326P 19980604, Provisional US 1998-88167P 19980605, Provisional US 1998-88202P 19980605, Provisional US 1998-88212P 19980605, Provisional US

1998-88217P 19980605, Provisional US 1998-88655P 19980609, Provisional US 1998-88734P 19980610, Provisional US 1998-88738P 19980610, Provisional US 1998-88742P 19980610, Provisional US 1998-88810P 19980610, Provisional US 1998-88824P 19980610, Provisional US 1998-88826P 19980610, Provisional US 1998-88858P 19980611, Provisional US 1998-88861P 19980611, Provisional US 1998-88876P 19980611, Provisional US 1998-89105P 19980612, Provisional US 1998-89440P 19980616, Provisional US 1998-89512P 19980616, Provisional US 1998-89514P 19980616, Provisional US 1998-89532P 19980617, Provisional US 1998-89538P 19980617, Provisional US 1998-89598P 19980617, Provisional US 1998-89599P 19980617, Provisional US 1998-89600P 19980617, Provisional US 1998-89653P 19980617, Provisional US 1998-89801P 19980618, Provisional US 1998-89907P 19980618, Provisional US 1998-89908P 19980618, Cont of US 2001-941992 20010828, US 2001-993604 20011114

FDT AU 2000037743 A Based on WO 200073454; EP 1210418 A1 Based on WO 200073454

PRAI WO 2000-US7377 20000320; WO 1999-US12252 19990602; US 1999-141037P 19990623; US 1999-143048P 19990707; US 1999-144758P 19990720; US 1999-145698P 19990726; US 1999-146222P 19990728; US 1999-149396P 19990817; WO 1999-US21090 19990915; WO 1999-US21547 19990915; US 1999-158663P 19991008; WO 1999-US28313 19991130; WO 1999-US28301 19991201; WO 1999-US30095 19991216; WO 1999-US30911 19991220; WO 2000-US219 20000105; WO 2000-US376 20000106; WO 2000-US3565 20000211; WO 2000-US4341 20000218; WO 2000-US4414 20000222; WO 2000-US4914 20000224; WO 2000-US5004 20000224; WO 2000-US5841 20000302; WO 2000-US6884 20000315; WO 1997-US20069 19971105; WO 1998-US19330 19980916; WO 1998-US19437 19980917; WO 1998-US21141 19981007; WO 1998-US25108 19981201; WO 1999-US106 19990105; WO 1999-US5028 19990308; WO 1999-US28634 19991201; WO 2000-US6319 20000310; WO 2000-US13358 20000515; WO 2000-US13705 20000517; WO 2000-US14042 20000522; WO 2000-US14941 20000530; WO 2000-US15264 20000602; WO 2000-US20710 20000728; WO 2000-US22031 20000811; WO 2000-US23522 20000823; WO 2000-US23328 20000824; WO 2000-US30952 20001108; WO 2000-US32678 20001201; WO 2001-US6520 20010228; WO 2001-US17800 20010601; WO 2001-US19692 20010620; WO 2001-US21066 20010629; WO 2001-US21735 20010709

IC ICM C12N015-12; C12Q001-68

ICS A61K038-17; C07H021-04; C07K014-05; C07K014-435; C07K014-47; C07K014-705; C07K016-18; C12N005-06; C12N009-00; C12N015-62; **C12P021-02**; G01N033-53

AB WO 200073454 A UPAB: 20030505

NOVELTY - An isolated nucleic acid (I) comprising 80 % identity to a sequence encoding one of 147 66-1165 residue amino acid sequences (S1), all fully defined in the specification and corresponding to PRO **polypeptides**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid comprising the full-length coding region of the DNA deposited as any of 141 ATCC accession numbers, given in the specification;

(2) a vector (II) comprising (I);

(3) a host **cell** (III) comprising (II);

(4) producing a PRO **polypeptides**, comprising culturing (III) under expression conditions, and recovering the **polypeptide**;

(5) an isolated **polypeptide** comprising at least 80 % identity to (S1) (IV), or to the extracellular domain of (S1)

(6) an isolated PRO **polypeptide** comprising at least 80 % identity to a sequence encoded by a nucleic acid deposited as any of the ATCC accession numbers of (1);

(7) a chimeric molecule comprising (IV) fused to a heterologous amino acid sequence;

(8) an antibody which specifically binds to a (IV);

(9) an isolated nucleic acid comprising at least 80 % identity to one of 147 236-3876 nucleotide sequences (S2), all fully defined in the

specification;
(10) an isolated nucleic acid comprising at least 80 % identity to the full-length coding region of (S2);
(11) an isolated extracellular domain of a PRO **polypeptide**, or a **polypeptide** having at least 80 % identity to its sequence;
(12) an isolated PRO **polypeptide** lacking its signal sequence, or having at least 80 % identity to its sequence;
(13) an isolated nucleic acid comprising at least 80 % identity to a sequence encoding (S1) or the extracellular domain of (S1);
(14) detecting a PRO943 or a PRO183, 184 or 185 **polypeptide** in a sample, comprising contacting the sample with PRO183, 184 or 185, or PRO 943, respectively, and determining the formation of a conjugate;
(15) the detection method of (14) for detecting PRO1133/PRO331, PRO363 or 5723/PRO363 or 1387, PRO1114/PRO3301 or 9940, or PRO1181/PRO7170, 361 or 846, by determining the formation of their conjugates;
(16) linking a bioactive molecule to a **cell** expressing PRO943, 183, 184, 185, 1133, 331, 363, 5723, 363, 1387, 1114, 3301, 9940, 1181, 7170, 361 or 846, comprising contacting the **cell** with a bioactive molecule bound to their appropriate PRO binding partner; and
(17) modulating at least one biologically activity of a **cell** expressing PRO943, 183, 184, 185, 1133, 331, 363, 5723, 363, 1387, 1114, 3301, 9940, 1181, 7170, 361 or 846, comprising contacting the **cell** with the appropriate PRO binding partner or the respective anti-PRO antibody.

ACTIVITY - Cytostatic.

Cells from human tumor **cell** lines were harvested with trypsin/EDTA, washed once, resuspended in IMEM (undefined) and their **viability** determined. The **cell** suspensions were added by pipet (100 micro l) into wells of a 96-well microtiter plate. Inoculates were allowed a preincubation period of 24 hours at 37 deg. C. The **cells** were diluted 1000-100000 fold and incubated for 6 days in a 5 % carbon dioxide atmosphere and 100 % humidity. After incubation, the medium was removed and the **cells** were fixed in 0.1 ml of 10 % trichloroacetic acid at 40 deg. C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4 % sulforhodamine B dye (Sigma) dissolved in 1 % acetic acid, rinsed four times with 1 % acetic acid to remove unbound dye, dried and the stain extracted for five minutes with 0.1 ml of 10 mM Tris base (tris(hydroxymethyl)aminomethane), pH 10.5. The absorbance of sulforhodamine B at 492 nm was measured using a computer-interfaced 96-well microtiter plate reader. No results are given.

MECHANISM OF ACTION - PRO agonist or antagonist.

USE - PRO **polypeptides** can be used for targeted delivery of bioactive molecules, such as **toxins**, radiolabels or antibodies, that cause **cell death** (Claimed). (I) can be used as hybridization probes, in chromosomal and gene mapping, and in the generation of anti-sense RNA and DNA. (I) may also be used to produce transgenic animals which are used to develop and **screen** therapeutically useful reagents. (IV) can be used as molecular weight markers in electrophoresis techniques.(I) and (IV) can be used for tissue typing. (IV) can be used to treat cancer. Anti-PRO antibodies can be used in diagnostic assays

Dwg.0/330

FS CPI EPI
FA AB; DCN
MC CPI: B04-C01G; B04-E03F; B04-E05; B04-E06; B04-E08; B04-F0300E; B04-F0900E; B04-F10A3E; B04-G01; B04-G21; B04-N02A0E; B04-P0100E; B11-C07A; B11-C08E2; B11-C08E5; **B12-K04A**; **B12-K04E** ; **B12-K04F**; B14-H01; B14-H01B; D05-C12; **D05-H09**; D05-H11A1; D05-H12A; D05-H12D1; D05-H12D2; D05-H12E; D05-H14A1; D05-H14A2; D05-H14B2; D05-H16A; D05-H17A6
EPI: S03-E14H4

TECH UPTX: 20010118
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: (I) comprises (S2), or its full length coding sequence.
Preferred Molecule: The heterologous sequence of the chimeric molecule is an epitope tag or an Fc region of an immunoglobulin.
Preferred Antibody: The antibody is a monoclonal, or humanized antibody, or is an antibody fragment.
Preferred Method: In the detection method, the sample comprises **cells** expressing the PRO **polypeptide**, and the detecting agent PRO **polypeptide** has a detectable label or is bound to a solid support. In the method of (16), the bioactive molecule is a **toxin**, radiolabel or antibody, and causes **cell death**. In the method of (17), the **cell** is killed.
Preparation: The antibodies specific for (IV) can be produced using standard hybridoma techniques.

ABEX UPTX: 20010118
WIDER DISCLOSURE - Disclosed as new are the following:
(1) agonists or antagonists to (IV);
(2) identifying antagonists or agonists of (IV), comprising contacting the PRO **polypeptide** with a candidate molecule and monitoring a biological activity mediated by the **polypeptide**; and
(3) a composition comprising (IV), an agonist or antagonist of (1) or an antibody specific for (IV), and a carrier.

SPECIFIC HOST CELLS - (III) is a Chinese hamster ovary cell, Escherichia coli cell or yeast cell (claimed).

ADMINISTRATION - (IV) are administered by e.g. injection or infusion intravenously, intraperitoneally, intracerebrally, intramuscularly, intraocularly, intraarterially, or intralesionally, or topically. The dosage of (IV) or its agonists or antagonists is 10 ng-100 mg/kg/day, preferably 1 micro-g-10 mg/kg/day.

EXAMPLE - No relevant examples are given.

L110 ANSWER 8 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2000-451677** [39] WPIX
DNC **C2000-137527**
TI **Peptide** fragments with **cell death** inhibitory activity, useful in preventing and treating apoptosis-associated diseases particularly caused by stress e.g. Parkinson's disease, Alzheimer's and arteriosclerosis.
DC B04 D16
IN HIRASHIMA, M; MAEDA, H; NOZAKI, C
PA (KAGA) CHEMO-SERO-THERAPEUTIC RES INST
CYC 23
PI WO 2000031131 A1 20000602 (200039)* JA 56p C07K014-47
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 2000011795 A 20000613 (200043) C07K014-47
EP 1132402 A1 20010912 (200154) EN C07K014-47
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000583957 X 20020305 (200232) C07K014-47
ADT WO 2000031131 A1 WO 1999-JP6322 19991112; AU 2000011795 A AU 2000-11795 19991112; EP 1132402 A1 EP 1999-972642 19991112, WO 1999-JP6322 19991112; JP 2000583957 X WO 1999-JP6322 19991112, JP 2000-583957 19991112
FDT AU 2000011795 A Based on WO 200031131; EP 1132402 A1 Based on WO 200031131; JP 2000583957 X Based on WO 200031131
PRAI JP 1998-347863 19981119
IC ICM C07K014-47
ICS A61K038-00; A61K038-17; A61P009-10; A61P025-16; A61P025-28; A61P031-18; C07K016-18; C12N005-06; G01N033-15; G01N033-50
AB WO 200031131 A UPAB: 20000818

NOVELTY - A **peptide** fragment or **peptide** group which has **cell death** inhibitory activity containing a defined 103 amino-acid sequence of residues in the C-terminal side of seleonprotein P, or an amino-acid sequence derived from that sequence but with some amino-acids deleted, substituted or added, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(i) a preventive or remedy composition for stopping deterioration of **pathogenesis** of diseases associated with apoptosis containing the **peptide** fragment or **peptide** fragment group as the main ingredient;

(ii) an additive for **cell** culture containing the **peptide** fragment or **peptide** fragment group;

(iii) a method for **screening cell death** activity by using a serum-free medium with 0.01-0.5% albumin added for studying the phenomenon of sudden **cell death** in a human megakaryotic series gemmule **cell** culture system by charging in the **peptide** fragment or **peptide** fragment group with evaluation of the degree of apoptosis; and

(iv) an antibody which can specifically bind to the **peptide** fragment or **peptide** fragment group as defined above.

ACTIVITY - Anti-AIDS; antiparkinsonian; antialzheimers; antisclerotic; cardiant; cardiovascular; cerebroprotective.

MECHANISM OF ACTION - **Cell death** inhibitor; antibody; selenoprotein P.

USE - The **peptide** fragments can be used as preventives and remedies for apoptosis-associated diseases particularly due to stress including acquired immunodeficiency syndrome (AIDS), Parkinson's disease, Alzheimer's disease and arteriosclerosis, cardiac infarct, cerebral infarct or organ transplant, re-perfusion damage, as well as relating to redox reaction or **cells** of the immune system, and as additive for **cell** culture and in **screening cell death** activity (claimed).

Dwg.0/10

FS CPI

FA AB; DCN

MC CPI: B04-B04L; B04-C01; B04-E03F; B04-E08; B04-F0100E; B04-N02A0E; B11-A; B11-C07A; B11-C08E1; B11-C09; **B12-K04A**; B12-M05; B14-F01; B14-F02; B14-G01B; B14-G02; B14-G03; B14-J01A3; B14-J01A4; B14-N16; B14-S03; B14-S11; D05-C12; D05-H07; **D05-H08**; **D05-H09**; D05-H11; D05-H12A; D05-H12E; D05-H14; D05-H17A6; D05-H18

TECH UPTX: 20000818

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Peptides**: The **peptide** is a partial sequence from one of 2 defined amino acid sequences given in the specification. The **peptide** fragment or **peptide** fragment group is especially originated from a plasma protein which is characterized by:

(a) recovering from a molecular weight fraction of 10-30 kDa;

(b) having a structure with isoelectric point at pH 7-8 in blood or isoelectric point of not less than 8 as studied by binding properties to ion-exchange resin;

(c) 2 bands in molecular weight 13-14 kDa and its sugar-chain adduct 2 bands in 16-17 kDa by non-reducing SDS-PAGE (sodium dodecyl sulfate polyacrylamide gel electrophoresis); or

(d) additional bands in 3-4, 7-9 and 10-12 kDa as for (c).

ABEX UPTX: 20000818

EXAMPLE - Into a serum-free medium SF03 (RTM) containing 0.05 muM 2ME and 0.1% BSA (bovine serum albumin) was added 1 ml subculturable Dami **cells** (1 x 106 **cells**/dish/3 ml) in 2 ml RPMI 1640/D-MEM/F-12 (1:2:2) mixed medium for culturing for 3 days before using for assay of **cell death** inhibition with a specimen.

Active fractions thus **screened** were purified for isolation of

useful **peptide** fragments.

L110 ANSWER 9 OF 11 WPIX (C) 2003 THOMSON DERWENT
AN **2000-072163** [06] WPIX
CR 2000-052761 [53]
DNC **C2000-020533**
TI Compositions for identifying apoptosis signaling pathway inhibitors useful for treating diseases.
DC B04 D16
IN INOHARA, N; KOSEKI, T; NUNEZ, G
PA (UNMI) UNIV MICHIGAN
CYC 77
PI WO 9955134 A2 19991104 (200006)* EN 89p C07H021-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9938702 A 19991116 (200015)
EP 1091980 A1 20010418 (200123) EN C07K014-715
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6348573 B1 20020219 (200221) C07K017-00
ADT WO 9955134 A2 WO 1999-US9183 19990427; AU 9938702 A AU 1999-38702 19990427; EP 1091980 A1 EP 1999-921504 19990427, WO 1999-US9183 19990427; US 6348573 B1 US 1998-69023 19980427
FDT AU 9938702 A Based on WO 9955134; EP 1091980 A1 Based on WO 9955134
PRAI US 1998-69023 19980427
IC ICM C07H021-00; C07K014-715; C07K017-00; C12Q001-68
ICS A61K038-00; G01N033-53; G01N033-567
AB WO 9955134 A UPAB: 20000203
NOVELTY - A purified protein (I) with a 531 residue amino acid sequence fully defined in the specification, is new. The sequence is the deduced sequence of the protein RICK.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a purified protein fragment which comprises amino acids 54-531, 248-531 or 365-531 of the 531 residue sequence (I); and

(2) a purified nucleic acid molecule encoding at least a fragment of (I);

ACTIVITY - None given.

MECHANISM OF ACTION - Activator. The RICK protein acts as a positive regulator of apoptosis, potentiating apoptosis induced by caspase-8 and caspase-10 during CD95 signaling.

USE - The invention provides methods for identifying apoptosis signaling pathway inhibitors and activators, and methods and compositions for **screening** compounds which will modulate the interactions of the various compositions identified: ARC, RICK, and the CIDE family of activators (CIDE-A, CIDE-B and DREP-1). RICK is useful in drug **screening** assays designed to identify drugs which interfere with the specific binding of RICK kinase to its substrate, or its activity, blocking downstream signaling. RICK is also useful in **screening** assays for agents or lead compounds for agents, useful in the diagnosis, prognosis or treatment of disease associated with excess **cell** growth and dysregulation of apoptosis. Complexes containing RICK and CLARP can be used in drug **screening** assays to identify inhibitor molecules blocking CD95-mediated apoptosis. Overexpression of ARC in an in vitro **cell** system can be used to identify inhibitors of the enzymatic activity of caspase-8. Identification of ARC-like inhibitory compounds may be useful for gene therapy treatment of disease with increased **cell death** in muscle tissue and cardiac disorders. Therapeutic compositions of CIDEs can be used to treat e.g. cancer, AIDS, neurodegenerative disorders, aplastic anemia, ischemic

injury, and **toxin**-induced liver disease. AntiRICK antibodies can be used as reagents for the preparation or affinity chromatography media, and for diagnostically measuring RICK levels.

ADVANTAGE - A specific inhibitor of an essential step in the biochemistry of apoptosis is needed. RICK interaction with intracellular factors such as CLARP and FADD appears to be essential for apoptosis, inhibitors of RICK binding to intracellular apoptosis factors are potential drug candidates.

Dwg.0/21

FS CPI

FA AB; DCN

MC CPI: B04-B03C; B04-E03F; B04-E08; B04-G07; **B12-K04**; **D05-H09**; D05-H11; D05-H12A; D05-H12D1; D05-H12E; D05-H14; D05-H17A

TECH UPTX: 20000203

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred protein: The purified protein is RICK (RIP-like interacting CLARP kinase) bound to a substrate which comprises CLARP or FADD. Preferably, the protein has an amino acid substitution at residue 38, which is the ATP-binding site, where the lysine residue is replaced by methionine.

Preferred fragment: The fragment is part of a fusion protein.

ABEX UPTX: 20000203

WIDER DISCLOSURE - Disclosed as new are:

(1) a vector which contains the nucleic acid of (2);

(2) a host **cell** containing the vector;

(3) a purified oligonucleotide capable of selectively hybridizing to the nucleic acid of (2) which may be labeled;

(4) complexes of ligands, such that a composition may comprise a RICK-kinase complex;

(5) an isolated nucleic acid molecule encoding at least a fragment of the apoptosis repressor protein (ARC);

(6) an isolated nucleic acid encoding at least a fragment of the human **cell death** inducing DFF45-like effector A (CIDE-A) protein; and

(7) anti-RICK antibodies.

ADMINISTRATION - No details are given.

EXAMPLE - To identify potential RIP-related genes, public databases of expressed sequence tags (ESTs) were searched for clones with homology to the catalytic domain of RIP. Three ESTs encoding the overlapping **peptides** were identified with significant amino acid homology to the kinase domain of RIP. Sequence analysis demonstrated that the longest cDNA clone had a 1.8kb insert and an open reading frame encoding a 531 amino acid protein, with a molecular weight of 60332Da. This protein was designated as RICK (RIP-like interacting CLARP kinase). Unlike RIP, the C-terminal region of RICK had significant similarity to the pro-domain of several caspases including caspase-1 and caspase-2. Northern blot analysis was performed to determine the distribution of RICK RNA transcripts in various human tissues. RICK was detected in heart, brain, placenta, lung, pancreas, spleen, lymph node and peripheral blood lymphocytes.

L110 ANSWER 10 OF 11 WPIX (C) 2003 THOMSON DERWENT

AN **2000-038501** [03] WPIX

DNN **N2000-029063** DNC **C2000-009798**

TI New bacterial **polypeptide**, useful for identifying antibiotic agents.

DC B04 D16 S03

IN ARIGONI, F; EDGERTON, M D; LOFERER, H; PEITSCH, M C

PA (GLAX) GLAXO GROUP LTD

CYC 86

PI WO 9954474 A2 19991028 (200003)* EN 50p C12N015-31

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZA ZW

AU 9937090 A 19991108 (200014) C12N015-31
ADT WO 9954474 A2 WO 1999-EP2640 19990420; AU 9937090 A AU 1999-37090 19990420
FDT AU 9937090 A Based on WO 9954474
PRAI GB 1998-8363 19980422
IC ICM C12N015-31
ICS C07K014-195; C07K014-395; C12Q001-68; G01N033-50
AB WO 9954474 A UPAB: 20000118
NOVELTY - An isolated **polypeptide** (PP) of the yihA gene family (A) is new.

DETAILED DESCRIPTION - An isolated (PP) of (A) as defined by:

(1) a high-scoring segment pairs (HSP) score of greater than or equal to 100 when compared with one of the sequences of (A) member, when the BLAST algorithm with a BLOSUM62 scoring matrix is used;

(2) containing a set of amino acid sequences which are positively identified when position dependent scoring matrices (PDMS) which is used to define (A) are used with MAST to yield a p-value of less than 1 multiply 10-30; or

(3) comprising any one of the following amino acid sequences in PROSITE patterns:

(I) Glu-Xaa(4)-Gly-(Gly Arg)-(Ser Thr Ala Gly)-Asn-Xaa-Gly-Lys-Ser-(Ser Thr Ala Gly);

(II) (Val Ile Leu Met)-Ala -Xaa(2)-Ser -Xaa(2)-(Pro Thr)-G-Xaa-T-(Arg Lys Gln Asn)-Xaa(2)-Asn-Xaa-(Phe Tyr).

Xaa = any amino acid

where the square brackets denote a single amino acid, the amino acids within the square brackets are alternatives and the number in the curved brackets refer to the number of residues at that position.

INDEPENDENT CLAIMS are also included for the following:

(1) a **polypeptide** or fragment comprising both of the sequences (I) and (II);

(2) a **polypeptide** containing any of the sequences set out in PDSM;

(3) an isolated polynucleotide encoding any one of the above **polypeptide**;

(4) a vector (V) comprising a transcriptional regulatory sequence and a nucleotide sequence encoding a (PP);

(5) a host **cell** comprising the above (V) and a reporter gene whose activity is linked to the expression of the (PP);

(6) an antagonist of a (PP) for use in therapy; and

(7) a method of treatment comprising administering the patient with an above antagonist.

(8) a method of assaying compounds for activity against bacteria comprising:

(a) contacting a (PP) fragment with an antagonist and measuring for binding to (PP) or **cell death**;

(b) expressing a (PP) or fragment in a host **cell** followed by contacting (PP) with an antagonist and measuring for inactivation of (PP);

(c) transfecting a host **cell** with a (V), allowing the host **cell** to express the (PN), increasing or decreasing the level of expression of (PP), measuring for binding (PP) and assaying for increase resistance or increased sensitivity to an inhibitor respectively; or

(d) generating a bacterial strain (BS) containing a reporter gene linked to the gene encoding a (PP), contacting (BS) with an antagonist and measuring for induction or inhibition of the marker.

USE - (PP) is useful in **screening** of antibiotic agents (claimed). Antagonists of (PP) are useful in therapy and for the manufacture of medicament for the treatment of bacterial infection

(claimed). (PN) molecules are useful as probes for other members of the gene family or in antisense therapy to block or to reduce the expression of one or more of the (PP). (PN) are also useful directly in **screening** and in generating whole **cell screens** by expression of a (PP).

ADVANTAGE - (PP)s are essential for the **viability** of a wide range of bacterial including both gram positive and gram negative bacteria hence antibiotics acting on a wide range of bacteria can be **screened**. Antagonists interfere with the initial physical interaction between a **pathogen** and mammalian host responsible for sequelae of infection and block the function of (PP) or (PN).

Dwg.0/5

FS CPI EPI

FA AB; DCN

MC CPI: B04-E02; B04-E08; B04-F0100E; B04-N03; **B12-K04**; **D05-H09**; D05-H12A; D05-H12E; D05-H14; D05-H17A6

EPI: S03-E14H4; S03-E14H5

TECH UPTX: 20000118

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Isolated (PN) is obtained by separation from their natural environment, preferably are provided in recombinant form and ideally purified to homogeneity.

Preferred Bacteria: **Polypeptide** is selected from Helicobacter pylori, Haemophilus influenza, Mycoplasma genitalium, Mycoplasma pneumoniae, Streptococcus pneumonia, Streptococcus pyogenes, Pseudomonas aeruginosa, Saccharomyces cerevisiae, Methanobacterium jannaschii, Neisseria gonorrhoea, Neisseria meningitidis, Staphylococcus epidermidis, Aquifex aeolicus, Bacillus subtilis and Escherichia coli.

Preferred **Polypeptide**: Fragments comprise alpha helix or alpha helix-forming region, beta sheet and beta-sheet forming region, turn and turn forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, amphipathic regions (alpha or beta), flexible regions, surface-forming regions, substrate binding regions and regions of high antigenic index.

Preferred Antagonist: The antagonist is a small organic molecule, a **peptide**, a **polypeptide**, antibodies, an antibody-derived reagent or chimeric molecules.

ABEX UPTX: 20000118

WIDER DISCLOSURE - The following are disclosed:

(1) variants, analogues and derivatives of (PP);

(2) variants, analogues and derivatives of polynucleotide (PN) which encode (PP)s;

(3) a polynucleotide having 70-90% identify with the above (PN); and

(4) a **polypeptide** having 70-90% identify with the (PP).

EXAMPLE - No relevant example given in the specification.

L110 ANSWER 11 OF 11 WPIX (C) 2003 THOMSON DERWENT

AN 1999-371143 [31] WPIX

DNC C1999-109609

TI Methods for determining gene essentiality useful in, e.g. preparation of conditional mutants.

DC B04 D16

IN JI, Y; MARRA, A; ROSENBERG, M

PA (SMIK) SMITHKLINE BEECHAM CORP

CYC 21

PI WO 9928508 A1 19990610 (199931)* EN 45p C12Q001-68

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP US

EP 1034308 A1 20000913 (200046) EN C12Q001-68

R: BE CH DE DK FR GB IT LI NL

JP 2002503447 W 20020205 (200212) 56p C12Q001-68

ADT WO 9928508 A1 WO 1998-US25808 19981204; EP 1034308 A1 EP 1998-962914 19981204, WO 1998-US25808 19981204; JP 2002503447 W WO 1998-US25808

19981204, JP 2000-523383 19981204
FDT EP 1034308 A1 Based on WO 9928508; JP 2002503447 W Based on WO 9928508
PRAI US 1998-105161P 19981021; US 1997-67446P 19971204; US 1998-82534P 19980420
IC ICM C12Q001-68
ICS C07H021-02; C07H021-04; C12N001-15; C12N001-19; C12N001-21; C12N005-10; C12N015-09; C12N015-64; C12N015-74; C12N015-75; C12N015-76; C12N015-77; C12N015-78; C12N015-79; C12N015-81; C12N015-85
AB WO 9928508 A UPAB: 19990806
NOVELTY - Methods for determining gene essentiality are new.
DETAILED DESCRIPTION - Determining gene essentiality comprises:
(a) transforming a group of host cells with a vector comprising an inducible gene control region expressibly linked to random polynucleotide sequences;
(b) inducing the inducible gene control region with an inducer; and
(c) detecting an alteration in the metabolism of the group of host cells.
INDEPENDENT CLAIMS are also included for the following:
(1) a method similar to above comprising:
(i) transforming a group of host cells with a library comprising an inducible gene control region expressibly linked to random antisense polynucleotide sequences;
(ii) inducing the inducible gene control region with an inducer; and
(iii) detecting killing or slowed growth of the group of host cells; and
(2) a method similar to (1) comprising:
(i) as in (1i) but where the control region expressibly is linked polynucleotide sequences;
(ii) as in (1iii) and (c); and
(iii) isolating the full length gene that comprises the coding sequence of a particular polynucleotide sequence or comprises the coding sequence of the complementary sequence of the selected polynucleotide sequence.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - The methods can be used to prepare conditionally expressed gene mutants, including conditional lethal mutants.
ADVANTAGE - None given.
Dwg.0/7
FS CPI
FA AB; DCN
MC CPI: B02-E; B02-T; B04-E06; B04-E08; B04-F0100E; B11-C08E1; **B12-K04F**; D05-H03; **D05-H09**; D05-H14
TECH UPTX: 19990806
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Host: The host **cell** is selected from:
(i) a prokaryote, member of the genus Streptococcus, Staphylococcus, Bordetella, Corynebacterium, Mycobacterium, Neisseria, Haemophilus, Actinomycetes, Streptomycetes, Nocardia, Enterobacter, Yersinia, Fancisella, Pasteurella, Moraxella, Acinetobacter, Erysipelothrix, Branhamella, Actinbacillus, Streptobacillus, Listeria, Calymmatobacterium, Brucella, Bacillus, Clostridium, Treponema, Escherichia, Salmonella, Klebsiella, Vibrio, Proteus, Erwinia, Borrelia, Leptospira, Spirillium, Campylobacter, Shigella, Legionella, Pseudomonas, Aeromonas, **Rickettsia**, Chlamydia, Borrelia and Mycoplasma, and further including a member of the species or group, Group A-G Streptococcus, S. pneumoniae, S. pyogenes, S. agalactiae, S. faecalis, S. faecium, S. durans, Neisseria gonorrhoea, N. meningitidis, Staphylococcus aureus, S. epidermidis, Corynebacterium diptheriae, Gardnerella vaginalis, Mycobacterium tuberculosis, M. bovis, M. ulcerans, M. leprae, Actinomycetes israelii, Listeria monocytogenes, Bordetella pertussis, B. parapertusis, B. bronchiseptica, Escherichia coli, Shigella dysenteriae,

Haemophilus influenza, Haemophilus aegyptius, Haemophilus parainfluenzae, Haemophilus ducreyi, Bordetella, Salmonella typhi, Citrobacter freundii, Proteus mirabilis, P. vulgaris, Yersinia pestis, Klebsiella pneumoniae, Serratia marcessens, S. liquefaciens, Vibrio cholera, Shigella dysenterii, S. flexneri, Pseudomonas aeruginosa, Franscisella tularensis, Brucella abortis, Bacillus anthracis, B. cereus, Clostridium perfringens, C. tetani, C. botulinum, Treponema pallidum, **Rickettsia rickettsii** and Chlamydia trachomitis;
(ii) an archaeon including Archaebacter; and
(iii) a unicellular or filamentous eukaryote, including but not limited to a protozoan, a fungus, a member of the genus Saccharomyces, Kluveromyces, or Candida,especially S. ceriviseae, K. lactis and C. albicans.
Preferred Genetic Materials: The inducible gene control region is an inducible promoter or an operator and inducible repressor. The polynucleotide sequence is an antisense sequence, selected from an organism as above. The vector comprises two inducible gene control regions, one expressibly linked to each terminus of the selected polynucleotide control sequence. The inducer is a chemical compound or electromagnetic radiation. The alteration in the metabolism is slowed **cell** growth, **cell death**, or **cell** stasis. The promoter is inducible by an inducer selected from, IPTG, doxycycline, erythromycin, tetracycline, and electromagnetic radiation. The antisense sequence comprises the complementary sequence of a gene expression control element. The gene expression control element is selected from a promoter, an enhancer, and a terminator. Each of the two inducible control regions is induced by a different inducer. The electromagnetic radiation is ultraviolet light, visible light, red visible light or green visible light.

ABEX UPTX: 19990806

EXAMPLE - In order to induce antisense RNA with the goal of downregulating virulence determinants and essential genes, a tet regulatory expression system was constructed in a shuttle vector. In S. aureus, this regulatory system showed a 70-fold level of induction in vitro and very strong dose dependence. It also functioned in vivo in a murine model of haemotogenous pyeloneohritis in combination with induction by oral administration of tetracycline. To determine whether induced antisense RNA could interfere with chromosomal gene expression, a 621 bp fragment of the alpha toxin gene (hla) was cloned downstream of this inducible promoter in antisense orientation, and was transduced into a clinical isolate of S. aureus. Antisense hla RNA inhibited expression of hla in S. aureus and showed a 14 fold decrease compared to the control. These results suggest that the tet regulatory system functions in vitro as well as in vivo and induced antisense RNA can downregulate chromosomal gene expression.

=> d his

(FILE 'HOME' ENTERED AT 11:30:42 ON 06 MAY 2003)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:30:49 ON 06 MAY 2003
E US20020192799/PN
L1 1 S E3
E WATOWICH S/AU
L2 25 S E4,E7,E8
E WEAVER S/AU
L3 17 S E3,E6
L4 40 S E30,E32,E33
E DAVEY R/AU
L5 36 S E3-E5,E25,E26
E CELL DEATH/CT
L6 6733 S E3-E5
E E3+ALL

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L7          1635 S E4
L8         54672 S E3+NT
L9         55879 S L6-L8
                 E PATHOGEN/CT
L10         2143 S E3
                 E E3+ALL
L11         3255 S E4,E3+NT
                 E PATHOGEN/CT
L12          822 S E9-E18
                 E E9+ALL
L13         1379 S E4,E3+NT
                 E PATHOGEN/CT
                 E E11+ALL
                 E E4+ALL
L14         5405 S E5
L15        19156 S E5+NT
                 E PATHOGEN/CT
                 E E13+ALL
L16           75 S E2
                 E E4+ALL
                 E PATHOGEN/CT
                 E E17+ALL
L17          248 S E2
                 E E4+ALL
L18        33475 S E6,E7,E5
L19        28931 S E5+NT
L20       317727 S (VIRUS OR VIRUSES OR BACTERIA OR BACTERIUM OR FUNGUS)/CW
L21        59879 S MICROORGANISM#/CW
                 E TOXIN/CT
L22        53134 S E3-E163
                 E E8+ALL
L23        74135 S E2+NT
L24        47106 S E48+NT OR E49+NT OR E50+NT OR E51+NT OR E52+NT OR E53+NT
L25          994 S E45+NT
                 E RICHETTSIA/CT
                 E RICKETTSIA/CT
L26         1173 S E3-E47
                 E E3+ALL
L27         1136 S E4+NT
L28         2052 S E3+NT
L29         3726 S L9 AND L10-L28
                 E DRUG SCREENING/CT
L30        18065 S E3-E5
                 E E3+ALL
L31        24177 S E2,E1
L32          215 S L29 AND L30,L31
L33          195 S L32 AND (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINO(L)ACID
L34          194 S L33 AND (PD<=20011015 OR PRD<=20011015 OR AD<=20011015)
L35            1 S L2-L5 AND L9
L36           48 S L2-L5 AND L10-L28
L37            1 S L2-L5 AND L30,L31
L38            1 S L1,L35,L37
L39            1 S L36 AND L38
L40           47 S L36 NOT L39
L41           65 S L2-L5 NOT L35-L40
L42           52 S L9 AND FUNGI/CW
L43           20 S L42 AND L30,L31
L44           18 S L43 AND (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINO(L)ACID
L45            1 S L44 NOT L34
L46          195 S L44,L34
                 E ANTIBACTER/CT
                 E E5+ALL
L47        94717 S E12-E14,E11+NT
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                E ANTIMICROB/CT
                E E6+ALL
L48       191636 S E4+NT
                E ANTIVIRAL/CT
                E E5+ALL
L49        38301 S E10,E11,E9+NT
                E ANTIFUNG/CT
                E E5+ALL
                E E2+ALL
L50        67685 S E9,E10,E8+NT
                E ANTITOXIN/CT
                E E4+ALL
L51         1449 S E4+NT
                E ANTIPATHOGEN/CT
L52           35 S L46 AND L47-L51
L53           34 S L52 AND (PHARMACOL? OR PHARMACEUT? OR BIOMOL?)/SC,SX
L54            1 S L52 NOT L53
L55           35 S L53,L54
L56           35 S L38,L55
L57           35 S L56 AND L1-L56
L58           58 S L6,L7 AND L46
L59           13 S L58 AND L47-L57
L60          124 S PROTEIN#/CW (L) (BUU OR USES)/RL AND L46
L61           17 S L60 AND L47-L51
L62            7 S L58 AND L61
L63           16 S L59,L61 NOT L62
                SEL DN AN 3 7 8 11 14 15
L64            6 S E1-E18
L65           13 S L62,L64
L66           12 S L57 NOT L61-L65
                SEL DN AN 2 4 5 6 10 11 12
L67            7 S E19-E39
L68           20 S L65,L67
L69         2064 S L26-L28
L70           15 S L69 AND L9
L71            2 S L70 AND L30,L31
L72            1 S L71 NOT PKC/TI
L73           20 S L68,L72
L74           13 S L70 NOT L71-L73
                SEL DN AN 1 4 5 8
L75            4 S E40-E51
L76           24 S L73,L75
L77           52 S L9 AND VERO
L78            0 S L77 AND L30,L31
L79            1 S L47-L51 AND L77
L80           51 S L77 NOT L79
                SEL DN AN 9 23 47
L81            3 S E52-E60
L82           27 S L76,L81 AND L1-L81
L83           27 S L82 AND (CELL(L)(DEATH OR SURVIV? OR REPLICAT? OR PROLIFERAT?

     FILE 'HCAPLUS' ENTERED AT 13:18:14 ON 06 MAY 2003

     FILE 'WPIX' ENTERED AT 13:18:30 ON 06 MAY 2003
                E US20020192799/PN
                E WATOWICH S/AU
                E WEAVER S/AU
L84           17 S E3,E5
                E DAVEY R/AU
L85            4 S E3,E4
L86           21 S L84,L85
                E RICKET
L87          613 S RICKET?/BIX
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L88       25585 S C12P021/IC,ICM,ICS
L89          53 S L87 AND L88

     FILE 'HCAPLUS' ENTERED AT 13:25:19 ON 06 MAY 2003

     FILE 'WPIX' ENTERED AT 13:25:39 ON 06 MAY 2003
L90      140542 S (Q233 OR N136)/M0,M1,M2,M3,M4,M5,M6
L91      133159 S (B12-K04 OR C12-K04 OR B12-K04A? OR C12-K04A? OR B12-K04E OR
L92          260 S L90,L91 AND L87
L93          264 S L89,L92
L94          127 S L93 AND ?PEPTIDE?/BIX
L95        22945 S  (CELL(L)(DEATH OR SURVIV? OR REPLICAT? OR PROLIFERAT? OR VIA
L96        15621 S L95 AND L90,L91
L97           64 S L96 AND L93
L98           44 S L97 AND L94
L99           24 S L98 AND C07K/IC,ICM,ICS
L100          34 S L98 AND C12N/IC,ICM,ICS
L101          37 S L99,L100
L102           4 S L97-L101 AND CELL DEATH/BIX
L103           4 S CELL DEATH/BIX AND L87
L104        1150 S CELL DEATH/BIX AND L90,L91
L105         443 S L104 AND SCREEN?/BIX
L106         262 S L105 AND ?PEPTIDE?/BIX
L107          40 S L106 AND (?PATHOGEN? OR ?TOXIN?)/BIX
                 SEL DN AN 3 5 10 24 28 30 32
L108           7 S E1-E16
L109          11 S L102,L103,L108
L110          11 S L109 AND L84-L109

     FILE 'WPIX' ENTERED AT 13:40:48 ON 06 MAY 2003
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